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OF

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St. Louis Children's Hospital

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400 S. Jefferson Ave.,
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American Journal of Diseases of Children

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SUMMARY OF FOUR YEARS OF CLINICAL AND BACTERIOLOGIC EXPERIENCE WITH MENINGITIS IN NEW YORK CITY*

PHEBE L. DuBOIS, M.D., AND JOSEPHINE P. NEAL, M.D.
NEW YORK

July 1, 1910, the preventive medicine annex of the Research Laboratory of the New York Board of Health took over the preparation, distribution and administration of antimeningitis serum from Rockefeller Institute. Jochmann, Kolle and Wassermann, the New York Board of Health and others had prepared the serum some time before it was taken up by Rockefeller Institute, so the serum itself was not new, but the credit for introducing its intraspinal use in this country is Dr. Flexner's. Under his direction, the Rockefeller Institute prepared it and distributed it to all who would supply careful records. This was of the greatest advantage in procuring a quick decision as to its great value. During part of the last big epidemic here (1904-05) the Health Department tried using it subcutaneously and found it to be of such doubtful value that its preparation was discontinued.

Meningitis is a reportable disease in New York City. The plan of the department from the first has been to have the physician on each case, so soon as he is known by the report of the case, offered the services of a department consultant.

We make our appointments with the attending physicians for the earliest moment possible and see cases nights and Sundays with them, because occasionally twelve hours' delay will seem to be a possible cause of a fatal outcome. We go over the history, examine the case, and if it seems to us to warrant it, even though we may not consider it to be one of meningitis, we do a lumbar puncture. It takes tact and infinite patience to persuade some of the poor, ignorant, foreign parents to allow us to do it, but usually if properly approached, they finally give in.

The conditions we have to consider mainly are epidemic or meningococcic meningitis, other purulent meningitides due most commonly in our experience to the streptococcus and pneumococcus and less

* Submitted for publication Nov. 12, 1914.

* From the Research Laboratory, Department of Health, New York City.

commonly to the *Streptococcus mucosus capsulatus* and influenza, tuberculous meningitis, poliomyelitis and meningism, particularly in pneumonia. We see many other conditions, as our yearly tabulations will show — sufficient, indeed, to make our work pleasantly exciting, for when a case is reported the probabilities are that it is not going to be epidemic cerebrospinal meningitis.

As a general thing, we do not go to see patients in hospitals. At first we thought such cases received proper treatment and did not need us, but as our knowledge of meningitis has increased and we have from time to time had occasion to observe such treatment and the results, we think hospitals would be wise to call us in once in a while to instruct the house staffs, for they are often left pretty much to their own devices, and though the serum treatment of meningitis is beginning to find its way into text-books the busy attending physicians have not had much occasion to learn about it and have little advice to offer.

The points of differentiation in their order of value among the above named conditions are in general, lumbar puncture with the examination of the fluid, the history and the physical signs.

A clear fluid increased in amount indicates usually one of the following conditions: tuberculous meningitis, poliomyelitis, syphilitic involvement of the central nervous system, brain tumor or meningismus. A cloudy fluid is the result of a meningitis due to the meningococcus or some of the other pyogenic organisms.

In examining fluids, we make both bacteriologic and chemical studies and when these are not conclusive inoculate guinea-pigs. We make smears and cultures from the sediment if fluids contain any. Other fluids are centrifuged for one hour at high speed and the smear made by putting the last few drops from the tube onto a slide and evaporating to dryness in the incubator. Smears from cloudy fluids are stained by Gram's method, those from clear fluids with Ziehl's tubercle bacillus stain. Occasionally it is necessary to make a capsule stain. In examining the smears we note the presence or absence of bacteria and the number and kinds of cells.

We have never counted the cells for two reasons: first, it is some time usually between the time fluids are withdrawn and the time that they are examined, for most cases are at some distance from the laboratory; secondly, we see no great advantage in doing it. We can tell from the stained sediment whether the cells are increased much, little, or not at all, and there is nothing particularly diagnostic in the exact number of cells per cubic millimeter. Moreover, since in most cases the cells are very few in number and it is impossible to use a large amount of fluid, no method can be very accurate. In poliomyelitis at the stage at which we usually see it, and in tuberculous and syphilitic

meningitis, the cells are considerably increased, there being from 20 to 30 to a field. Mononuclears predominate up to 95 per cent. often. In epidemic cerebrospinal meningitis and the meningitides due to other pyogenic organisms the cells are enormously increased, so much so that it is not necessary to centrifuge. The polymorphonuclear leukocytes predominate, often up to 98 per cent. at first. Later, if the condition improves, the cells decrease and gradually the percentage of mononuclears increases.

The cultures are made after the smears are examined. Those showing *Streptococcus pyogenes, Streptococcus mucosus capsulatus* or meningococcus, or those in which no organism is found, but one of these is suspected of being the cause, are planted on 2 per cent. glucose ascitic agar. Those showing influenza or pneumococcus are planted on blood agar. Clear fluids are always injected subcutaneously in from 5 to 7 c.c. amounts into the groins of a guinea-pig. The pig is kept for a month and then injected in the axilla with 1 c.c. of crude tuberculin diluted to 3 c.c. with normal saline. Usually if it is tuberculous it is dead next morning. For proof of tuberculosis we depend on caseous inguineal glands or tubercles in the spleen or both at necropsy. Clear fluids that have become contaminated will sometimes produce enlarged inguinal glands that may even go on to caseation, but 1 c.c. of tuberculin will not kill in those cases.

We make chemical tests for albumin, globulin and reduction with Fehling's solution. For albumin, we use the nitric acid ring test and judge of the amount of albumin by the depth of the ring when it is first formed. The globulin test is that of Noguchi and is made by adding to one part of the fluid four or five parts of 10 per cent. butyric acid made up in normal saline, boiling, adding about as much normal sodium hydroxid as there was fluid to begin with and boiling again. Too much sodium hydroxid spoils the test by redissolving the globulin. Normal fluids will give a very faint opalescence; pathologic fluids a flocculent precipitate varying in amount with the severity of the inflammation present. Fluids showing globulin are said to be the result of inflammation of the meninges and we have never had reason to doubt it. Indeed, to us it is the most important of the chemical tests, because it separates fluids due to meningism from those due to a true meningeal infection. Both the albumin test and the globulin test are of course worthless, if there is blood present. The majority of clear fluids reduce Fehling's solution. The statement is now and then made that a differential point in diagnosis between tuberculous meningitis and poliomyelitis is the fact that poliomyelitis fluids will reduce Fehling's solution, but tuberculous fluids will not. We have tried Fehling's reaction with eighty-eight known tuberculous fluids and sixty-five, or 73 per

cent., gave good reduction. So, while the absence of reduction is of marked significance, the presence of reduction means absolutely nothing. The fluid from a case of heat prostration also failed to reduce Fehling's. In cloudy fluids it is not uncommon to find the reduction present if the case is seen early and is mild, then to go through a period where there is no reduction, and as the patient improves and the fluid clears, to have it return. In making the test we use equal quantities of Fehling's solution and spinal fluid.

We have examined two fluids and have seen a third that illustrated the syndrome of Froin. This is characterized by spontaneous coagulation and a yellow color. The pathogenesis of this condition is not known except, of course, that some hemorrhage has taken place. The two fluids we examined were from poliomyelitis patients, one of whom recovered and one died. The third fluid was from a patient with epidemic cerebrospinal meningitis supposed to have had a fracture of the skull. This patient recovered.

Table 1 is a concise statement of the various characteristics of the different fluids.

From July 1, 1910, to July 1, 1914, we examined 992 cerebrospinal fluids. Included with those we withdrew are some sent in by physicians who made their own punctures. Our method of examination and the differential points have already been discussed. We have found that examinations of fluids from epidemic cerebrospinal meningitis are more apt to be successful if done promptly, as the meningococcus sometimes autolyzes in twelve hours so that they will not grow and are very difficult to distinguish by smear. As cases recover the organisms are found more and more within the cells, and they usually show in spreads after the cultures become negative.

In examining for tubercle bacilli, we find the sediment after prolonged centrifuging at high speed better adapted to our purposes than the examination of the fibrin web. As our fluids are brought to the laboratory from varying distances, the formation of the web is disturbed; frequently, too, we wish to examine a fluid without allowing time for the web to form. By this method we get positive results in about 65 per cent. of cases. This is not nearly so high a percentage as that obtained by Dr. Hemingway at the Babies' Hospital using the web, but she was able to make several punctures, if necessary, while we rarely see a case of tuberculous meningitis more than once.

The history is of importance in the purulent meningitides, for, though they are differentiated from each other only by microscopical and cultural examinations, a history of middle-ear disease or fracture of the skull makes us suspect that some other than the meningococcus is the infecting organism. In differentiating between tuberculous

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meningitis and poliomyelitis the history is of more importance than the examination of the spinal fluid if tubercle bacilli are not found, because the chemical and microscopic pictures are so frequently identical in the two conditions. In poliomyelitis there is usually the history of a sudden onset with a very high temperature dropping quickly. There may have been prodromata; gastro-intestinal disturbance is common, and many cases show redness of the throat or some involvement of the upper respiratory tract, but they are so slight that it takes careful questioning to elicit them. The history of a tuberculous case, on the other hand, is usually that of an insidious onset preceded by unusual irritability, though occasionally we see children in families in which they have been carefully observed that give a history of a sudden onset, frequently with convulsions. Usually the temperature has been between 99 and 101 F.; occasionally it will have been normal or subnormal. Transient paralyses, projectile vomiting and crying out in the night are frequently mentioned. Given a patient in apparent coma, usually a determined effort will rouse the child with poliomyelitis and he will answer intelligently, though afterward he sinks back immediately into stupor. It is impossible to rouse the tuberculous child in the stuporous stage.

The differentiation between epidemic cerebrospinal meningitis and tuberculous meningitis is usually comparatively easily made. Cases of epidemic cerebrospinal meningitis usually give a history of a sudden onset as against a slower onset in tuberculous meningitis. The patient's mental condition usually remains good in meningococcic meningitis unless it is a fulminating case. In tuberculous meningitis the history is commonly that of irritability followed by increasing stupor from which it is impossible to arouse the child. Patients with epidemic cerebrospinal meningitis show marked rigidty of the neck; tuberculous patients are apt to have slight or moderate anterior-posterior rigidity, but none laterally. In infants the rigidity of epidemic cerebrospinal meningitis is so easily overcome as to make one often doubt its existence, but when the infant is turned on the side the head is markedly retracted. The fever is higher in epidemic cerebrospinal meningitis, and runs an irregular course. Projectile vomiting is common in tuberculous meningitis and rare in epidemic meningitis.

Very few luetic or other chronic conditions of the central nervous system or meninges come to our attention, but we do see a good many cases of meningism. By meningism we mean that condition in which meningeal symptoms arise in the course of some disease, the cerebrospinal fluid being increased in amount but normal in character. Some difference of opinion exists in regard to the use of the term. It was introduced by Dupré, who considered it a functional disturbance.

Other writers have used the term serous meningitis, pseudomeningitis, meningitis sine meningitide and meningitis infectiosa circumscripta or circumscribed meningitis. This latter term is considered preferable by Plaut, Rehm and Schottmüller. Holt describes a case which showed at necropsy a circumscribed meningitis. Huber in an article on "Pneumococcus Meningitis and Meningism," inclines to the opinion that the pathologic basis is a localized inflammation, usually of infectious origin.

In the face of this evidence we cannot deny that cases exist in which the clinical picture and the increased fluid is due to a circumscribed infection, but from our experience it seems to us highly improbable that this is always or even often the case.

We have seen 80 cases of which the outcome in 53 was recovery and in 22 death, while with 5 the outcome is unknown. The diseases which the meningism accompanied are as follows:

Pneumonia—uncomplicated	39
Gastro-intestinal disease	8
Whooping-cough (two patients had pneumonia also)	6
Scarlet fever (one patient had pneumonia also)	5
Typhus	3
Typhoid complicated by pneumonia	1
Measles	1
Middle-ear disease	1
Retropharyngeal abscess	1
Orbital abscess	1
Pott's disease	1
Epilepsy	1
Rachitis	1
Streptococcus osteomyelitis	1
Staphylococcus septicemia	1
Influenza	1
Nephritis	1
Heat prostration	1

Of the 22 patients who died, 8 died within twenty-four hours, and were desperately ill when seen. Of the 14 living longer than twenty-four hours, 4 died of pneumonia (in 1 two punctures were made with normal fluid in each instance), 1 of gastro-intestinal disease, 1 of whooping-cough complicated with bronchopneumonia, 3 of scarlet fever (1 complicated by bronchopneumonia and diphtheria, and 1 very septic), 1 of typhoid complicated by pneumonia, 1 of staphylococcus septicemia (two punctures done with normal fluid, one of streptococcus osteomyelitis—necropsy showed normal brain and meninges), 2, cause unknown.

In most of these cases the meningeal symptoms did not progress. Had they done so, a second puncture would have been made. In two cases, as noted, second punctures were done revealing normal fluids. In all cases the severity of the accompanying disease or diseases was quite sufficient to account for death. Of course, this by no means proves the absence of a localized meningeal infection. We have never

seen a case of generalized meningitis following a case of meningism, however, which we should expect to see occasionally considering the number under observation, were there a localized infection of the meninges, and in view of the relatively large number of patients that recover promptly, we believe that in most cases the condition is a functional one, probably of toxic origin.

In sixty-nine of these cases lumbar puncture was done. In the other cases we did not do a puncture, either because the symptoms had cleared up considerably when the case was seen or because with the accompanying disease we felt sure the case was one of meningism and advised waiting. Latterly, we have done a lumbar puncture even though we have felt sure it was meningism, as the withdrawal of the fluid seems to hasten recovery.

Of course, the amount of fluid depends on the stage of the condition at which the puncture is done. We have withdrawn very large amounts — from 80 to 100 c.c. In other cases the amount has been little increased above normal. It is commonly accepted that in a true meningitis the fluid is inflammatory in character — of the nature of an exudate. Such a fluid shows an increase in albumin and globulin and in the number of cells. In a meningism, as we use the term on the other hand, the fluid is of the nature of a transudate. Except in the cases noted below, the cells have not been increased, neither has the albumin and globulin content, and Fehling's has been readily reduced. In all cases they have been negative bacteriologically, by smear culture and animal inoculation.

In two cases of pertussis, the patients dying the same day the puncture was done, there was some increase in albumin and globulin and number of cells, in one case about equally divided between endothelial cells and polynuclears, in the other 95 per cent. or more polynuclears. These changes were presumably ante mortem. In one case of typhus the cells were increased — 95 per cent. mononuclears. This patient recovered. The case of heat prostration showed a faint increase in albumin and a slight increase in cells, 70 per cent. being polynuclears. This fluid, as has been stated before, failed to reduce Fehling's, though repeated tests were made, and was the only fluid that did not do so readily. The patient recovered.

Plaut, Rehm and Schottmüller include under the term "meningism" cases with spinal fluid in which there is an increase in albumin and globulin and in number of cells usually mononuclear, sometimes polynuclear. We feel that such instances may be mild and recovering cases of epidemic cerebrospinal meningitis in which the organism has cleared up before the puncture was made. We have seen several cases ourselves in which from the clinical history, the progress of the case and

the character of the fluid we were convinced of the diagnosis, while we were unable to prove it bacteriologically.

In examining patients, we particularly note the following points: the presence or absence of MacEwen's sign or in infants a bulging fontanelle; the eyes (whether or not the pupils are dilated, contracted or unequal, presence of conjunctivitis, strabismus, nystagmus, etc.); the mental condition (whether there is delirium, irritability or stupor); the presence or absence of Kernig's and Brudzinski's signs; regularity in rate and depth of respiration and rate and volume of pulse; the reflexes (whether they are increased, diminished or absent); the temperature and presence or absence of an eruption. Of these signs we consider the stiffness of the neck, the variation of regularity in rate and

TABLE 1.—CHARACTERISTICS—

Meningeal Condition	Pressure	Amount c.c.	Appearance	Cytology
Normal	Normal	5-10	Clear	Very few cells
Meningismus	Increased	10-100	Clear	Very few cells
Poliomyelitis	Increased	20-100	Clear; sometimes slight fibrin web	Early polynucleosis; later lymphocytosis up to 95 per cent.; endothelial cells
Tuberculous meningitis	Increased	30-120	Clear fibrin web	Lymphocytosis up to 95 per cent.
Epidemic cerebrospinal meningitis	Increased	5-120	Cloudy	Polynucleosis up to 98 per cent.
Meningitis due to other organisms	Increased	20-100	Cloudy	Polynucleosis up to 98 per cent.

depth of respiration and MacEwen's and Brudzinski's signs the most important. MacEwen's sign consists of a change from the normal in the percussion note over the lateral ventricles due to increased intraventricular pressure. It takes some practice to appreciate it. Brudzinski's sign consists in the flexion and eversion of the legs and arms when an attempt is made to flex the head on the chest. Wherever we have found a MacEwen we have always obtained increased fluid, except in cases of basic meningitis, in which case the connection between the brain and cord is partially or totally cut off.

The mental condition is frequently good in epidemic cerebrospinal meningitis unless the case is of the fulminating type. Early in tuberculous meningitis there is irritability, later stupor. In poliomyelitis irritability not followed by stupor is the usual thing.

Conjunctivitis is fairly common in epidemic cerebrospinal meningitis and rare in other meningeal conditions. Ptosis and strabismus are

more common in tuberculous meningitis, but may occur in other meningeal conditions.

We do not attach much significance to Kernig's sign, because it is difficult to make sure of it in young children. Brudzinski's sign is of much greater value to our minds.

In true meningitis the depth and time between respirations is markedly irregular, the so-called Biot's breathing. Late, particularly in tuberculous meningitis, the respiration frequently becomes Cheyne-Stokes. The pulse is more apt to be irregular in rate and volume in tuberculous meningitis than in other meningeal conditions.

Palsies are uncommon in epidemic cerebrospinal meningitis; in 112 cases we have seen palsy twice only. It is common, but usually transi-

—OF THE VARIOUS FLUIDS

Bacteriology	Albumin	Globulin	Fehling's Solution	Animal Inoculation
Sterile	±	±	+	Negative
Sterile	±	±	+	Negative
Sterile	+—++	+—++	+	Negative
Tubercle bacilli	++—+++	++—+++	— in 25 per cent.	Tuberculosis in four weeks
Meningococcus	++—++++	++—++++	+ or — according to severity and stage	
Infecting organism	++—++++	++—++++	— may be + early	

tory in tuberculous meningitis, and always present in frank cases of poliomyelitis.

As has already been stated, the temperature in general is low and long continued in tuberculous meningitis, is high, rising rapidly and dropping quickly in poliomyelitis and runs a very irregular course in epidemic cerebrospinal meningitis.

Eruptions aside from herpes are not very common in our experience, though in times past epidemic cerebrospinal meningitis has been known as spotted fever. In 112 cases we have seen an eruption sixteen times. In cases in which it did occur there was nothing characteristic about the eruption itself, its location or the time of its appearance or disappearance.

Table 2 shows the number of cases from July 1 of one year to July 1 of the next year for the last four years.

The increase in numbers from year to year has been partly due to the gradual spread of the knowledge that such work is being done. We regret that even after four years there are many physicians in New York who are entirely unaware of the existence of our department. Aside from that, we feel that there has been a real increase in the number of cases of epidemic cerebrospinal meningitis. It is a disease for which apparently the majority of individuals have a natural immunity. Many healthy people carry meningococci in their noses and throats for long periods of time, acquiring them either from cases or from carriers. After a certain length of time, when there has been

TABLE 2.—NUMBER OF CASES BY YEARS, JULY 1, 1910, TO JULY 1, 1914*

	1910-1911	1911-1912	1912-1913	1913-1914	Total
Epidemic cerebrospinal meningitis	17	25	29	41	112
Tuberculous meningitis	22	44	37	51	154
Other meningitides	11	7	11	18	47
Anterior poliomyelitis	1	25	16	5	47
Pneumonia	6	8	16	22	52
Other diseases	14	30	20	53	117
	71	139	129	190	529

* Some few of the cases during the first two years were seen only by Dr. Sophian, who had charge of the work during that time.

TABLE 3.—NUMBER OF CASES DURING THE FOUR QUARTERS OF THE YEAR

	July-October	October-January	January-April	April-June
1910-1911	..	5	3	9
1911-1912	6	4	10	5
1912-1913	4	6	9	10
1913-1914	2	4	16	19
	12	19	38	43

little meningitis about, a new generation of susceptible individuals comes on the scene. These, with possibly certain meteorologic factors which we do not understand, probably determine epidemics to a large extent. It has been about ten years since the beginning of the last epidemic. With the increasing number of cases another epidemic may be approaching. Fortunately, this last year it has been of a mild type.

Table 3 gives the number of cases during the four quarters of each year. The greatest number of cases occurs between March 1 and June 1 each year.

Table 4 shows the number of physicians with whom we have consulted and the number of cases we have seen with each.

There are 531 instead of 529 cases, because in two instances there were two physicians in charge of cases, and in order to make the number of physicians come out right it was necessary to count each of these cases as two.

TABLE 4.—PHYSICIANS CONSULTED AND CASES SEEN

Physicians	No. of Cases Seen with Each	No. of Cases Seen
254	1	254
60	2	120
10	3	30
8	4	32
8	5	40
4	6	24
1	7	7
3	8	24
348		531

The treatment of epidemic cerebrospinal meningitis resolves itself into prophylaxis and specific and general treatment. The prophylaxis consists in quarantining patients ill with the disease and those in contact with them who show meningococci in cultures from the nose and throat. Under ordinary circumstances epidemic meningitis is not very highly contagious, but it sometimes becomes so. We have seen more than one case in a family in only four instances. The first time a child of 11 had it and three months later her mother had it. Both recovered. The second time two brothers, adults, were sick in the same room. Most insanitary conditions prevailed. The first brother had been ill two weeks and had had no doctor. The second was a fulminating case and the patient died in three days. The first one was sent to a hospital and finally died after five weeks' illness. In the third instance, a brother and sister, adults, and the 8-year-old daughter of the sister were all ill in the same apartment. The brother and sister were taken ill within two hours of each other and both died. The little girl was taken five days later and recovered. The day before the little girl was taken sick a neighbor, a man living in the same house came down with it and eventually recovered. The fourth instance was that of a sister of 14 and a brother of 3½. The sister had been taken sick two days before the boy. The attacks were mild and both recovered.

The question of carriers is rather a difficult one. In the first place, it requires careful bacteriologic technic to isolate meningococci from nose and throat cultures when they are few in numbers, and the work cannot be left to laboratory assistants unless they have exceptional training. When there are many cases to be diagnosed and treated is the time when nose and throat cultures from carriers come in thick and fast, and until quite recently we have not had a sufficiently large force to manage the cultures satisfactorily. From some work done here two years ago, we think the most satisfactory method of dealing with carriers is to swab out the nose and throat two or three times daily with 20 per cent. argyrol. We hope to do more work along this line this winter. Hatchel and Hayward report success with a spray of antimeningococcic serum and with subcutaneous injections of meningococcus vaccine.

The specific treatment consists in the intraspinal administration of antimeningitis serum. This is a specific immune serum of therapeutic value only in meningococcic meningitis and then only when administered subdurally. In making a lumbar puncture we do not use either general or local anesthesia. We think that general anesthesia is dangerous, and local anesthesia takes so much preparation and time that the overcoming of the pain does not compensate for the increased nervous tension on the part of the patient. Adults not acutely ill who submit to lumbar puncture for diagnostic purposes do not seem to mind much. The back is not very sensitive, and if the patient is held properly — lying on the side with the knees drawn up against the abdomen, the neck bent and the back well arched so that the intervertebral spaces will be as great as possible — and the operator is skilful there is very little pain. Never under any circumstances do we do it with the patient sitting up. Iodin is used over about 4 square inches immediately around the point of election for puncture and a sterile or bichlorid towel is laid over the hips through which to find the landmarks. We have never to our knowledge had a secondary infection of the meninges of the cord. Sometimes the skin has become infected in small children from soiled napkins. We use a Quincke needle size 18 or 19, and go in the mid-line through the notch most nearly coinciding with a line drawn from crest to crest of the ilium. A piece of tubing about 15 inches long is attached to the metal connection that fits in the end of the needle when the stylet is withdrawn. To the other end of the rubber tubing is attached the barrel of a syringe. We usually cut the rubber and insert a short piece of glass tubing near the metal connection so that we can see the fluid flowing out or the serum flowing in. It is well to attach the tubing in removing the fluid because by raising and lowering the glass container the

rapidity of outflow can be regulated. A too sudden decrease in intracerebral pressure is undesirable. When the fluid withdrawn is cloudy we always inject antimeningitis serum at once even though we suspect that some other organism may be the cause. The serum does no harm no matter what the organism may be, and if it is meningococcic meningitis the earlier serum is administered the better. Later treatment depends on the examination of the cerebrospinal fluid. We have used streptococcus and pneumococcus serums in appropriate cases. No patient with pneumococcus meningitis directly under our supervision has recovered, but we know of two patients who did. One patient with streptococcus meningitis out of fifteen recovered, but no influenzal patient. At present we have a good supply of anti-influenzal serum furnished us by Dr. Flexner, and as cases come along we shall use it.

As stated above, if the first fluid is cloudy we inject antimeningitis serum. It is warmed to body temperature and injected very slowly by gravity under the least possible pressure. This method was introduced by Koplik. A syringe is dangerous, and is probably responsible for many deaths following the administration of serum. In general, the dose for an adult is from 20 to 40 c.c., and for infants and children from 3 to 20 c.c. The amount depends as much on the quantity of cerebrospinal fluid withdrawn as on the age. An infant will frequently stand 20 c.c. without difficulty. The dose should usually be at least 5 or 10 c.c. less than the amount of cerebrospinal fluid withdrawn.

We have seen a number of cases of undoubted dry taps during the course of cases of meningococci meningitis. The serum ran in freely and showed the usual variation in movement depending on respiration. In such cases it is advisable to proceed very slowly and to watch the patient carefully for the slightest change in pulse and respiration. We think that possibly in some cases the exudative period is followed for a short time by one of decreased secretion. At any rate, a dry tap is frequently followed by one in which fluid is obtained. In cases with thick exudate that will not flow through the needle, gentle suction with a syringe may be tried. If that fails a little serum injected will sometimes start the flow. In very severe cases we inject the serum every twelve hours until there is improvement. In moderate and mild cases we usually repeat it each day for the first four days. Further administration depends on the patient's general condition and the bacteriologic examination of the fluid. Usually from 4 to 6 injections are necessary, but we have employed as many as sixteen or more. We consider that we get better results if the patient is turned from side to side so that no two successive punctures are done with the patient lying on the same side. That insures the emptying of the lateral ventricles in rotation.

A number of times during or immediately after the injection of serum the patient has gone into shock. Respiration has become slow and shallow or ceased, the facies pale and pinched and the pulse rapid and thready. At first this was very alarming, but we have never had a patient die from it. If the needle is still in place we withdraw some of the serum. Artificial respiration is resorted to if breathing has ceased and hypodermic stimulation is given for the heart. We have seen it happen much less frequently since we have been using smaller doses.

The serum we have been using lately contains 0.2 per cent. trikresol; earlier it contained 0.3 per cent. As is well known, the trikresol has been blamed by several physicians, especially Dr. Kramer of Cincinnati, for the fatal results that have been reported in a few instances following the injection of antimeningitis serum, usually in young children. Hale, of the Hygienic Laboratory at Washington, and Auer, of Rockefeller Institute, report experiments with dogs showing that serum containing trikresol is somewhat more toxic than unpreserved serum or that containing chloroform or ether. Auer carried on experiments with monkeys also, and showed that they were far less sensitive to trikresol serum than the dogs. Furthermore, in France, where serum without preservative is used, cases of shock and occasional fatal results are reported. As stated above, we have never seen such a case, although we have administered the serum considerably over five hundred times and to children of all ages, fourteen of our patients being under a year old. In view of our experience with serum that has always contained trikresol, we cannot believe that it is the cause of the fatalities. We think rather, that they may be due to injudicious administration of the serum — too large doses, or too rapid increase of pressure, which is likely to happen unless the gravity method is used — or to an unusual susceptibility on the part of the patient. On account of the fear of trikresol — unfounded, we feel — that has been produced by these reports, it seems advisable to try for a while the use of chloroform or a preservative. A comparison of the results with the serum prepared with the two different preservatives will enable us to decide which method is preferable.

We have not given the method of administering serum with the use of the blood-pressure apparatus a fair trial because we have so seldom had sufficient assistance to manage it. We think it is probably a help to those who have had little experience.

If a case shows a tendency to become chronic we make an autogenous vaccine and give it every four or five days in doses of from 250 to 1,000 million. Sometimes it has seemed to be very effective, but we have not had enough cases to be able to draw definite conclusions. We can say that we have never seen it do any harm. In treating cases it

must be remembered that frequently the stiff neck is the last symptom to disappear and if the fluid has cleared up and the temperature stays down it may be entirely disregarded.

The use of hexamethylenamin (urotropin) comes between general and specific treatment. We recommend its administration in all acute meningeal infections. It is said that twenty minutes after its administration formaldehyd can be detected in the spinal fluid. It may not be there in sufficient amounts to do much good, but the procedure seems rational. The fact that meningococci may be isolated from the urine is another argument for its use. In one case of *Streptococcus mucosus capsulatus* meningitis we gave hexamethylenamin dissolved in normal saline intraspinally. The temperature dropped from 106 F. to 102 F., and the patient became rational, but the case terminated fatally.

In planning the general treatment we find it necessary to remember that epidemic cerebrospinal meningitis may be a greatly prolonged febrile disease. The patient is best kept in a quiet darkened room. Sedatives are needed if the patient is very restless. We have had one fatal prolonged case in which we thought the patient might have been saved had the doctor given her an opiate so that she might occasionally have had a few hours of rest. The bowels and bladder should receive careful attention, particularly the bladder. Retention and cystitis are not uncommon. The patient should be examined for a distended bladder daily and the family warned to report infrequency of micturition. Patients should not lie in a draught and should be carefully covered up, especially during and after puncture. We have learned by bitter experience how easily they fall victims to pneumonia. In ordering the hygiene of the sick-room it must be remembered that the meningococci are found in the secretions of the nose and throat and in the urine. The diet should be such that it may be easily digested but generous in amount. The high caloric diet of typhoid is indicated for the reason that meningitis-like typhoid may be prolonged. The ice-bag gives a measure of relief for the headache.

Among the complications we have had:

Pneumonia in	7 cases
Basic meningitis in	6 cases
Paralysis in	3 cases
Hydrocephalus in	3 cases
Deafness in	3 cases
Cystitis in	2 cases
Serum rash in	2 cases
Iritis in	2 cases
Typhoid in	1 case
Scarlet fever in	1 case
Measles in	1 case
Purulent otitis media in	1 case
Blindness in	1 case
Arthritis in	1 case

In no case of basic meningitis under our care has recovery ever ensued. At first we used to try very hard to get the patients into hospitals to have brain puncture done. Now we explain to the family that it may do some good, but do not urge it strongly because we do not feel that it is of much avail. Of the cases with paralyses, two cleared up. One case of deafness cleared up entirely after the lapse of several months. The patients with typhoid and measles both recovered. We are much interested in the question of mental deterioration following meningitis and are following up our cured patients. In the course of time we shall have sufficient data from which to draw conclusions.

Table 5 shows our mortality statistics for the four years from July 1, 1910 to July 1, 1914.

TABLE 5.—MORTALITY, JULY 1, 1910, TO JULY 1, 1914

Year	Total No. Cases	Patients Recovered	Patients Died	Result Unknown	Mortality Per Cent.
1910-1911	17	10	7	0	41
1911-1912	25	7	15	3	60
1912-1913	29	17	12	0	41
1913-1914	41	30	11	0	26

The 1911-1912 statistics need some explanation: four cases developed into basic meningitis and in five other fatal cases the patients were either in hospitals already or were sent there and we had slight oversight of the treatment.

We feel that this particular department — meningitis — is a worthwhile venture in treating cases of meningitis, in teaching physicians whom we see in consultation to administer serum and in training a group of experts who will be able to handle efficiently the outbreaks of meningitis that occur about every ten years in New York City.

THE LANGE GOLD CHLORID REACTION ON THE CEREBROSPINAL FLUID OF INFANTS AND YOUNG CHILDREN *

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This paper contains the results of the Lange reaction on the spinal fluids of some sixty odd children and infants. We are reporting these because of the evidence that the colloidal gold reaction is of undoubted value as an aid in the early diagnosis of many cerebrospinal diseases occurring in such patients.

The first work on colloidal gold was that done by Michael Faraday[1] in 1857. His colloidal solutions were made by reducing gold chlorid with phosphorus. It was not, however, until 1898 that Zsigmondy[2] devised the present-day method for making clear solutions or suspensions of colloidal gold. He gives several methods for making these gold hydrosols. The first method is the one used in making the indicator for our tests. Briefly, a dilute solution of gold is mixed with potassium carbonate and reduced at the boiling-point by formaldehyd.[3] If clear red solutions are desired, which can be used as colloidal reagents, then the details as described in previous work must be followed.[4] Zsigmondy further showed that on the addition of most electrolytes the red color quickly changes to a blue, and then deposits gold as an extremely fine powder.[5] Another phenomenon discovered by him was that the presence of foreign colloids of certain kinds present the color change as well as the precipitation of gold. Even 0.0001 per cent. of gelatin is enough to do this. This phenomenon he designates *Goldschutz,* which for each albuminous body is quantitatively different. Each albuminous body, then, has a definite gold figure (*Goldzahl*) reckoned in terms of the number of milligrams necessary to protect 5 c.c. of goldsol against precipitation by 0.5 cm. of 10 per cent. sodium chlorid.[6] It was further noted that 1 c.c. of

* From the Children's Wards of the Cook County, Presbyterian and Provident Hospitals, and the Laboratories of the Presbyterian and St. Luke's Hospitals.

1. Faraday, Michael: Proc. Roy. Soc., 1857, viii, 356; Phil. Mag., 1857, iv, 13, 401.
2. Zsigmondy: Ann. d. Chem. (Liebig's), 1898, ccci, 30.
3. Zsigmondy and Alexander: Colloids and the Ultramicroscope, Chap. viii.
4. Sippy and Moody: Trans. Am. Phys., 1913, p. 720. Grulee and Moody: Jour. Am. Med. Assn., 1913, lxi, 13.
5. Zsigmondy and Alexander, Chap. iii, p. 78.
6. Zsigmondy and Alexander, Chap. iii, p. 79.

0.4 per cent. sodium chlorid would have no effect on colloidal gold. Then, if one diluted the serum in 0.4 per cent. sodium chlorid a point would be reached at about 1:1,500 which is the optimum dilution of globulin to precipitate out the goldsol, whereas, if this dilution is made with distilled water there is no optimum dilution point.

With this as a basis Carl Lange[7] in Wechselmann's laboratory in Berlin set out to apply the principle in testing pathologic spinal fluids. At that time he was interested primarily in the spinal fluids of syphilitics whom Wechselmann was treating by the salvarsan method. The technic as worked out by Lange is briefly as follows:

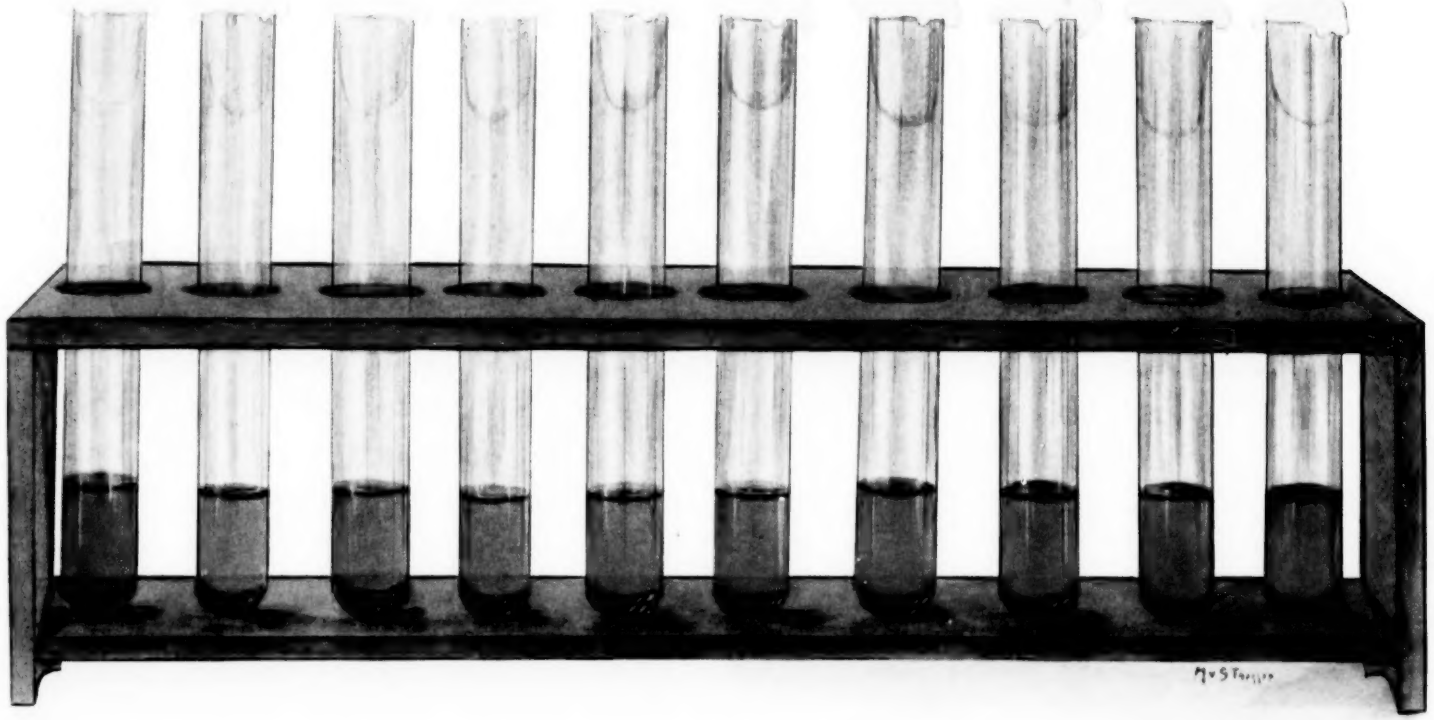
TECHNIC OF GOLD CHLORID REACTION

A series of test-tubes (6 by ¾ in size) is used. In the first tube place 1.8 c.c. of a 0.4 per cent. sodium chlorid solution (freshly made from a stock 10 per cent. solution), and 1 c.c. in each of the succeeding nine. Then take 0.2 c.c. of the spinal fluid to be tested and add to the first tube, thus making a dilution of 1:10. This is mixed with a 1 c.c. pipet. One c.c. is removed and added to a second tube, making a dilution in this tube of 1:20. This procedure is carried on throughout the series, the remaining quantity being thrown away. When the dilutions are finished there is 1 c.c. in each tube, and the dilutions vary from 1:10, 1:20, 1:40, 1:80, etc., up to 1:5,120 in the last tube. Then add rapidly to each tube 5 c.c. of the indicator, which is a colloidal solution of gold.

As stated above, it is the making of the indicator that requires the greatest amount of care, because there are many small but important factors necessary to observe absolutely in order to obtain a useful indicator. Briefly, we may say that absolute chemical cleanliness and the following of the technic in detail as it is described is the only possible way to obtain the best indicator. A good indicator is necessary for accurate results from the test. The indicator when good is absolutely clear, is red in color, with some yellow and a tinge of purple. If kept in a clean Jena glass flask away from the light it will remain unchanged for months.

The tests when made should stand for twenty-four hours to get the maximum amount of reaction before taking a final reading. Nevertheless, one can within fifteen to thirty minutes, and in many cases sooner, tell what the result will be. This is especially true of any strong reaction. For convenience and to facilitate the reading and interpretation of the results obtained by the test in general, the reactions may be divided into three groups. The first group includes the reactions which are strongest in dilutions of 1:40 and 1:80 (third and fourth tubes). Second group, those having maximum reactions in the fourth, fifth and sixth (1:80, 1:160, 1:320) tubes; third group,

7. Lange, Carl: Ztschr. f. Chem. u. verwandte Gebiete, 1913, i, No. 1, pp. 44-78.



The usual reaction of the Lange gold chlorid test on the cerebrospinal fluid in congenital syphilis.

Illustrating Article by C. G. Grulee, M.D., and A. M. Moody, M.D.
American Journal of Diseases of Children, January, 1915.

the reactions which are strongest in the seventh to tenth (1:640 to 1:5,120) tubes.

The diseases of the brain and cord falling into the first class are those due to syphilis, that is, syphilitic meningitis, gumma of the brain, tabes dorsalis, general paresis and congenital syphilis. In all of these the maximum reaction is in the third and fourth (dilutions 1:40 and 1:80) tubes. These involve certain variations which will be taken up later. Syphilitic meningitis, gumma of the brain, as well as congenital syphilis, give, as a rule, a red-blue or violet color. This would be designated as a 2 reaction. Tabes dorsalis early in the disease or after treatment might give the same type of reaction. In a well-developed tabes, however, there is usually a 3:5 (dark to light blue or water white) reaction at 1:40 and 1:80 with the reaction fading gradually to the left and rather abruptly to the right. General paresis gives, even early in the disease, a reaction typical for that condition alone. So constant is the reaction that one may venture a diagnosis without other findings either clinical or laboratory. This reaction is the strongest of them all and in it we see an absolutely clear, colorless fluid (5) in the first four, five or even as high as the eighth tube, with a (2) reaction in the tenth tube. A taboparetic spinal fluid early would react strongly — approaching very closely the reactions for a true general paresis.

The reactions in the second group are rarely stronger than a dark blue (3) and usually lie between a red-blue and a violet (2 to 3). Tuberculous meningitis usually gives the strongest reactions of any of this group. The point of maximum reaction is usually in the fifth and sixth (dilutions 1:160 and 1:320) tubes. As the disease progresses it may approach the higher dilutions. In two cases of this series in which the spinal fluid was tested shortly before death occurred, the maximum reaction was in the eighth tube (1:1,280). In this respect it resembles the reaction occurring in suppurative meningitis. Brain tumors, toxic meningitis (meningismus), edemas from sunstroke, uremia, etc., may give a slight reaction of equal intensity in the fourth, fifth and sixth tubes (1:80, 1:160 and 1:1,320) when they react at all. Brain tumors in the presence of normal spinal fluid give no reaction.

All stages of acute encephalitis on to brain abscess belong also in this second group. The reaction approaches more nearly that for syphilis than any other type of lesion. The maximum reaction is usually in dilutions of 1:80 and 1:160, but extending toward the higher dilutions, thus differing from syphilis.

Suppurative meningitis from any cause will give a strong reaction in the higher dilutions, usually strongest in the seventh and eighth

tubes (1:60 and 1:1,200). This is usually a dark blue color (3), but may be so strong that a clear, colorless (5) reaction will occur.

Group colloidal gold reactions for syphilis and tuberculous meningitis have been reported more recently by Eicke[8] and Lee and Hinton.[9]

Miller and Levy[10] conclude that the Lange reaction "is of no aid in the diagnosis of purulent or tuberculous meningitis," and that "it has no advantage over known laboratory procedures in the diagnosis of congenital syphilis." After reading the results recorded in their paper, we do not believe that they have drawn proper conclusions. They report 100 per cent. positive Wassermann reactions in congenital syphilis cases, however. We have been unable to get such results.

The following precautions were taken in obtaining the cerebrospinal fluid: After sterilization of the puncture needle it was thoroughly cleansed with alcohol and then with ether; the skin was washed with iodin and the iodin removed with alcohol. All fluids were rejected in which blood could be recognized. The Wassermann reaction, when tested, was made on the cerebrospinal fluid, unless otherwise mentioned in the tables. We might state that we were strongly impressed by the fact that in congenital syphilis a rather florid state of the disease is required to produce a positive Wassermann reaction.

Table 1 is a report of eighteen cases of congenital syphilis. It will be seen that in every one of these cases there was a definite precipitation in the gold chlorid solution. This reaction in every case showed its greatest intensity in the dilutions of 1:40 and 1:80. In only one instance, Case 14, was there any reaction above the dilution of 1:320. In Case 3 and Case 9, after, respectively, seven weeks and one year of treatment, the reaction was materially altered, in Case 3 no reaction appearing, and in Case 9 the reaction being very markedly reduced.

Table 2 contains reactions of four infants. These reactions are peculiarly similar to those obtained in paretic dementia in adults. It is for that reason that they have been separated from the cases tabulated in Table 1.

It will be noted that in all these cases in the first six dilutions the precipitate was great, and that in the first case the precipitate was almost complete throughout. In Cases 1, 2 and 3 death occurred in from five days to two months after the examination of the cerebrospinal fluid, but unfortunately in none of these cases could a necropsy be obtained.

8. Eicke. München. Med. Wchnschr., 1913, lx, 2713-2717.
9. Lee and Hinton: Am. Jour. Med. Sc., 1914, cxlviii, 33.
10. Miller and Levy: Bull. Johns Hopkins Hospital, 1914, xxv, No. 279, 133.

TABLE 1.—CONGENITAL SYPHILIS

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Harold G.	3 wks.	+	..	—	2	2	2	2	1	0	0	0	0	0	
2. Helen W.	6 wks.	+	..	—	3	3	3	3	3	0	0	0	0	0	
3. Anna K.	6 wks.	±	..	..	2	3	2	2	0	0	0	0	0	0	
Anna K.	13 wks.	..	..	..	0	0	0	0	0	0	0	0	0	0	After 7 weeks' treatment.
4. James McK.	2 mos.	—	..	—	0	1	1	0	0	0	0	0	0	0	
5. Vincent W.	2 mos.	+	..	—	1	2	3	3	1	0	0	0	0	0	
6. Louisa W.	3 mos.	—	..	.	0	1	2	2	0	0	0	0	0	0	
7. Baby M.	4½ mos.	—	..	+	2	3	2	2	0	0	0	0	0	0	
8. Louise C.	5 mos.	+	..	..	0	1	1	1	1	0	0	0	0	0	
9. Baby C.	6 mos.	+	..	..	3	4	5	4	2	1	0	0	0	0	After 1 year's treatment.
Baby C.	18 mos.	—	..	—	0	1	1	0	0	0	0	0	0	0	
10. Ruth S.	6½ mos.	+	..	+	0	2	3	3	1	0	0	0	0	0	
11. Baby Ma.	7 mos.	—	..	..	0	1	1	1	0	0	0	0	0	0	
12. Mary M.	9 mos.	—	..	..	2	3	3	2	1	0	0	0	0	0	
13. Gertrude R.	10 mos.	±	..	..	1	2	3	3	1	1	1	0	0	0	
14. Joe C.	11 mos.	?	..	..	1	1	2	2	3	1	0	0	0	0	
15. Armando M.	1 yr.	—	..	..	2	3	3	3	1	0	0	0	0	0	
16. Nick L.	1 yr.	—	..	..	1	2	3	3	0	0	0	0	0	0	
17. Olga A.	2½ yrs.	+	.	+	1	1	4	4	3	1	0	0	0	0	
18. Baby E.	4 yrs.	+	..	—	2	3	5	4	1	0	0	0	0	0	

TABLE 2.—REACTION LIKE THAT OF PARETIC DEMENTIA

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Eva R.	7 mos.	++++	..	..	5	5	5	5	5	5	4	4	4	4	Death within 1 week.
2 Thomas C.	11 mos.	++	20	+	5	5	5	5	4	3	2	0	0	0	Death in 5 days.
3. Dorothy H.	13 mos.	++	..	..	5	5	5	4	4	1	0	0	0	0	Death in 2 months.
4. Florence R.	8 yrs.	++	70	+	5	5	5	5	4	3	2	1	0	0	Many symptoms of paretic dementia.

Patient 4 was a little girl of 8 years who entered the Presbyterian Hospital July 19, 1913, on the service of Dr. Bassoe. The history was as follows: Father and mother were well; three younger brothers, all healthy, normal and strong; there was one premature birth, the first child, with death three weeks after birth; after this a miscarriage at seven months; then the patient was born, and after her the three boys above mentioned. There is no family history of imbecility, idiocy, etc.; no history of tuberculosis or syphilis. The child had measles and mumps when a year old, but up to the fifth year she was apparently perfectly normal and then she began slowly to show signs of idiocy. This began by running over a lot of words which had no sense to them. She gradually developed incontinence of feces and urine. She recognized only her parents and brothers; she did not cry much, ate well and had no pain. She was nervous; her knees seemed weak; her right arm was weaker than the left and was slowly getting worse. She was easily frightened but slept soundly. On physical examination the pupils of the eyes were found large and reacted slowly to light; nose and ears negative; teeth irregular; thyroid was not to be palpated; there were no abnormal findings in the chest or abdomen. As to the extremities, it was noticed that the fingers of the right hand were somewhat overextended, especially in the end phalanges. Reflexes: Pupils reacted very slowly to light; the patellar reflex was exaggerated; Achilles and arm reflexes were present and there was some question as to the Babinsky. As to her speech, it was found that some of the common things she could say very well, and this would be followed by words which made no sense.

There is enough in this history to make one at least strongly suspicious of the presence of a paretic dementia, even though this condition is quite rare at this age.

As to the interpretation of the other three cases, it is impossible for us to offer any suggestions. It seems, however, that investigation of such cases is well worth future study.

Table 3 contains twelve cases which we were not able to show positively clinically were congenital syphilis. There was, however, in every case a strong suspicion. It will be noted in this series, too, that with the exception of Case 6, reaction was most marked in the dilutions of 1:40 and 1:80.

Patient 6, Grant R., entered the Presbyterian Hospital on the service of Dr. Grulee on May 27, 1914, aged 1 year. He came in with the complaint that the present trouble began with a cold in the head and croup six weeks before. During the previous week the condition had been getting much worse; breathing was difficult and wheezy. The child had never been cyanotic. The stools were green and contained curds, and there was no vomiting. The child had been breast-fed up to three or four days before entrance; had never been previously ill; there was very marked dyspnea on expiration and inspiration. The child cried seldom but its cry was hoarse. There was marked retraction of the lower end of the sternum; in the sternal region there was diminished resonance and flatness which extended one finger's breadth to the left of the sternum; over the whole chest breath sounds were loud and wheezy; bronchophony over the spine within one finger's breadth of the lowest level of the spine of the scapula; no fine râles.

In the abdomen the spleen was found to be two fingers' breadth below the ribs and was firm; the liver was not enlarged. The cervical axillary and inguinal glands were enlarged but no epitrochlears were felt. Examination of the larynx by Dr. Friedberg showed a subglottic swelling which was probably

TABLE 3.—SUSPECT CONGENITAL SYPHILIS

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Helen C.	6 wks.	±	..	..	1	2	4	5	4	1	0	0	0	0	
2. Irene N.	3 mos.	+	..	+	1	2	3	3	1	0	0	0	0	0	
3. Vladimir	5 mos.	—	..	..	1	2	3	3	1	0	0	0	0	0	Also tetany.
4. Peter L.	9 mos.	—	..	..	0	3	3	2	1	0	0	0	0	0	
5. Forrest S.	9 mos.	±	..	..	0	0	1	0	0	0	0	0	0	0	Severe anemia.
Forrest S.	11 mos.	±	..	..	1	2	3	3	1	0	0	0	0	0	Severe anemia.
6. Grant R.	1 yr.	—	12	—	0	1	1	0	0	0	0	0	0	0	
7. Walter R.	15 mos.	—	..	..	0	0	1	1	0	0	0	0	0	0	
8. Ethel F.	18 mos.	+	..	..	3	3	3	1	0	0	0	0	0	0	
9. Nick N.	18 mos.	+	..	.	0	0	1	1	0	0	0	0	0	0	
10. Wyd. St.	2 yrs.	±	..	+	2	3	5	4	1	0	0	0	0	0	
11. Gladys	2¾ yrs.	±	..	..	2	2	3	2	1	0	0	0	0	0	
12. Mart. B.	3 yrs.	—	..	+	3	5	5	5	2	0	0	0	0	0	

TABLE 4.—TUBERCULOUS MENINGITIS

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Ralph B.	2½ mos.	—	71	..	1	1	2	4	4	3	1	0	0	0	Questionable; symptoms typical.
2. Madeline R.	4 mos.	++	..	..	0	0	0	1	1	3	4	3	0	0	
3. Irene P.	7 mos.	—	..	..	0	0	0	0	2	3	4	4	2	0	
4. Harry K.	18 mos.	++	150	—	0	0	2	3	5	5	4	1	0	0	
5. Harold B.	3 yrs.	++	..	..	2	2	3	4	5	3	1	0	0	0	
6. Blanche G.	3 yrs.	++	..	..	3	3	3	4	5	5	1	0	0	0	
7. Roy A.	4½ yrs.	—	..	..	1	1	2	3	4	4	2	1	0	0	
8. Charles S.	.....	+	57	+	1	1	1	2	2	1	0	0	0	0	Syphilitic meningitis.

an edema. The blood showed 3,560,000 reds, 17,900 whites, and 50 per cent. hemoglobin (Dare).

The child rapidly improved on a powder consisting of mercury with chalk, ½ grain, and sodium bromid, 2 grains, given three times a day. The child left the hospital on June 7 much improved, and from recent reports, on continuing the same treatment the improvement has been steady. The Roentgenogram showed a shadow in the mediastinum which appeared to be a mass of enlarged mediastinal glands. Whether this is a case of congenital syphilis or not, we do not feel competent to say.

Among these cases were two, Cases 5 and 11, in which a severe anemia was gradually but materially benefited by mercurial treatment.

SUMMARY

Summing up the gold chlorid reaction as it occurs in congenital syphilis, it seems to us that the following may be stated:

There are two types of reaction which occur in cases of congenital syphilis; one in which the height of the reaction is obtained in the dilutions of 1:40 and 1:80; in higher dilutions there is a distinct tendency to less reaction, and this reaction never continues past the dilutions of 1:640, and infrequently past the dilutions of 1:160. The second reaction approaches closely that of paretic dementia and needs further investigation before it can be properly interpreted.

Table 4 contains the reactions in eight cases of tuberculous meningitis. In five of these cases the reaction was most marked in the dilutions of 1:160 and 1:320. In two the reaction was greatest in dilutions of 1:640 and 1:1,280; in one at 1:40 and 1:80. In Case 2 the diagnosis of miliary tuberculosis with tuberculosis of the meninges was confirmed at necropsy.

The diagnosis of Case 1 is questionable, principally because of the age. No signs of general miliary tuberculosis were to be found. The case may have been one of syphilitic meningitis. The child left the hospital and it was impossible to trace it further. There is little question that there is marked reaction of the colloidal gold chlorid solution to the cerebrospinal fluid in tuberculous meningitis.

Very few conclusions may be drawn from such a small series of cases. In five of the eight cases the reactions were most marked in the dilutions of 1:160 and 1:320. It is a noticeable fact, however, that in two cases the reaction was most marked in the dilutions of 1:640 and 1:1,280, the same as in the case of septic meningitis, Table 5, Case 3. After examination of the cerebrospinal fluid in tuberculous meningitis in adults, we have come to look on the first-noted reaction as the more typical and almost never to expect reaction in dilutions of 1:640 and 1:1280 except in cases of septic meningitis.

In Table 5 are included those cases in which there were symptoms of conditions affecting the mentality or meninges. In this have been

TABLE 5.—OTHER CEREBRAL CONDITIONS

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Benny T.	2⅓ yrs.	+	14,700	..	0	1	2	3	2	1	0	0	0	0	Pneumococcus (?) meningitis.
2. Charles N.	1 yr.	+	..	+	0	0	0	0	1	1	0	0	0	0	Pneum. Mening. (necropsy).
3. Sarah R.	3 mos.	+++	..	..	1	1	1	1	3	4	4	3	1	1	Septic meningitis.
4. Edwin B.	21 mos.	?	..	..	1	2	4	3	2	0	0	0	0	0	Meningismus Susp. of Syph.
5. Dale H.	7 yrs.	..	..	..	1	1	2	1	0	0	0	0	0	0	Pneum. and meningismus.
6. Homer B.	9 yrs.	?	38	—	1	2	3	3	1	0	0	0	0	0	Meningismus (?).
7. Jake P.	5 yrs.	?	2	—	1	2	3	2	0	0	0	0	0	0	Hydrocephalus.
8. Michael M.	5 yrs.	—	..	..	0	0	0	0	0	0	0	0	0	0	Cretinism.
9. John Z.	7 yrs.	..	..	..	0	0	1	2	2	2	0	0	0	0	Cretinism.
10. Marie B.	8 mos.	+	..	+	2	2	2	2	1	0	0	0	0	0	Agenesis of brain with edema ex vacuo; no signs of syph. at necropsy.
11. Tony R.	6 yrs.	..	..	..	0	1	1	0	0	0	0	0	0	0	Idiocy following encephalitis.

TABLE 6.—OTHER CONDITIONS

Name	Age	Nonne	Cell-Count	Wassermann	Lange Gold Chlorid Dilutions										Remarks
					1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120	
1. Edmund D.	2 yrs.	..	..	—	0	1	0	0	0	0	0	0	0	0	Pneumonia.
2. Charles S.	9 mos.	0	..	..	2	2	3	0	0	0	0	0	0	0	Lobar pneumonia.
3. John C.	23 mos.	.	..	..	0	0	0	0	0	0	0	0	0	0	Intoxication.
4. Frank D.	10 mos.	..	..	..	0	0	0	0	0	0	0	0	0	0	Intoxication.
5. Theodore H.	16 mos.	..	..	∓*	0	0	0	0	0	0	0	0	0	0	Absolutely no signs of syphilis; decomposition.
6. Thomas C.	3 mos.	..	.	..	1	2	2	2	1	0	0	0	0	0	Decomp. and otitis media.
7. Tina M.	9 mos.	..	..	—	4	4	4	4	0	0	0	0	0	0	Decomp. and acute nephritis.
8. Katina K.	2½ mos	..	.	..	0	1	1	0	0	0	0	0	0	0	Pylorospasm.
9. Infant A.	5 mos.	..	..	..	1	2	3	3	2	1	0	0	0	0	Prematurity.
10. Vladimir	6 mos.	?	.	.	0	0	1	1	0	0	0	0	0	0	Miliary tuberculosis.
11. Anna R.	1 yr.	+	2	+	1	1	1	1	0	0	0	0	0	0	Tumor of the parotid.

* Negative in spinal fluid, positive in blood.

included two cases of cretinism. In Cases 1, 4, 5, 6, 7 and 10, the reaction is seen to be similar to that of congenital syphilis. Case 1 was a case of meningitis due to diplococci, probably pneumococci. Case 4 was a case of meningismus in which there were strong suspicions of congenital syphilis. Cases 5 and 6 were also cases of meningismus but in neither of these cases was there any reason to suspect syphilis. Case 7 was a case of chronic hydrocephalus, probably of congenital origin. Case 10 was a case of idiocy in which the Wassermann and gold chlorid tests were both positive for syphilis, but which at necropsy showed nothing anatomically which would bear out this diagnosis.

The difference in the reactions of the cerebrospinal fluid in the two cases of cretinism is worthy of notice. Case 9 was far more advanced than Case 8. Whether this accounts for the greater reaction, it is impossible to say.

It is to be noted that in Case 2, while the Nonne and Wassermann were distinctly positive, the reaction to the gold chlorid was slight.

Table 6 contains eleven cases in most of which the patients were examined to obtain fluids which could be used as controls. It will be noted that four of these showed reactions which corresponded to the reactions of congenital syphilis. Of these, one, Case 11, gave at the same time a positive Wassermann reaction. Patient 9 was a premature baby and some suspicions of syphilis may attach to it. Case 10 was a case of miliary tuberculosis with distinct signs of involvement of the meninges. Case 7 was one of severe marasmus in a Greek baby 9 months old. The child had no certain enlargement of the spleen; there was, however, a mass in the left upper abdominal region which might have been an enlarged spleen. The epitrochlear glands were enlarged in addition to this, and the child showed marked involvement of the kidney which was rather in the nature of a severe pyelocystitis than of a nephritis. There were some points in this which might suggest the possibility of a congenital syphilis; at least its presence cannot be absolutely ruled out.

It should be stated that the amount of cerebrospinal fluid obtained was in many instances too small for use in making the cell count and Wassermann reaction after the Nonne and gold test had been made

CONCLUSIONS

1. In the cases of congenital syphilis included in this report the cerebrospinal fluid reacted to the colloidal gold chlorid solution always in the lower dilutions, and with a marked degree of regularity strongest in the dilutions of 1:40 and 1:80.

2. There is a small group of cases of congenital syphilis in which the reaction is similar to that of paretic dementia.

3. The reaction as obtained in congenital syphilis is most nearly approached by those conditions which show a slight inflammation of the meninges or brain and are not likely to be confused clinically with syphilis.

4. The reaction in tuberculous meningitis is found to be most intense in the dilutions of 1:160 and 1:320. It is likely that the more rapid the course the more apt is the reaction to occur in the higher dilutions.

5. From the foregoing statistics it is evident that the Lange gold chlorid reaction is of value only as an aid in diagnosis.

In addition to the references in the preceding text the following may be referred to:

Kaplan, D. M., and McClellan, J. E.: Jour. Am. Med. Assn., 1914, lxii, 511.

DeCrinis, Max, and Eberhardt, Frank: München. med. Wchnschr., 1914, xxii, 1216.

Smith, L. D.: Illinois Med. Jour., 1914, xxvi, 420.

Brock, G. W.: Illinois Med. Jour., 1914, xxvi, 422.

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ACIDOSIS WITH AUTO-INTOXICATION IN INFANTS AND CHILDREN

A STUDY OF ONE HUNDRED CONSECUTIVE CASES IN APPARENT EPIDEMIC FORM *

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Between Nov. 18, 1913, and Feb. 1, 1914, in Concord, N. H., and its immediate neighborhood, there were approximately two hundred cases of illness associated with the presence of acetone bodies in the urine. They were diagnosed as cases of acidosis, and while some were doubtless of an inconsequential type that would ordinarily have escaped detection, the majority showed definite symptoms of severe auto-intoxication — symptoms wholly out of proportion to any obvious organic cause. Sporadic cases of acidosis in children, with auto-intoxication and recurrent vomiting, are not rare in that city; but it appeared that in this instance we had to deal with the disease in epidemic form. There were nine fatalities.

I have tabulated 102 consecutive cases, two of which were in women, aged, respectively, 38 and 36. If we eliminate these women we are left with an even hundred cases in infants and children. In the two adults the histories and symptoms were quite analogous to those portrayed in the larger group.

But three infants out of a hundred were less than a year old. Eight were between 1 and 2 years. The great bulk of the patients — eighty in all — were fairly evenly distributed among the ages from 2 to 8. Then came a few scattering cases up to 13, the age of the oldest child. There were 59 boys and 41 girls — a deviation from the accepted ratio.

In view of the fact that Concord is a well-to-do city with comfortable homes, one would expect that the majority of the afflicted children would be well nurtured. Twenty of the homes I have listed as fair, the remainder as good or excellent. None were distinctly poor. Either tenements were notably exempt or else their quota escaped detection.

The earliest cases were discovered at Penacook, five miles from Concord, the middle of November. On December 1 a case was reported

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* Read before the Annual Joint Meeting of the New England Pediatric Society, the Philadelphia Pediatric Society, and the Pediatric Section of the New York Academy of Medicine at the Academy of Medicine, New York, Nov. 5, 1914.

at Boscawen, 10 miles distant, and later in the month children were taken ill at Canterbury, 10 miles away in another direction. The first case to be diagnosed in Concord itself occurred on December 1. The fact that a wide territory was involved has a distinct bearing on water and milk as causative factors, for both of these were procured from a variety of sources. In Concord, the city water analyzed exceptionally well; milk came from at least a dozen dealers. In the surrounding towns both milk and water came, as a rule, from the farms on which the patients lived. Two infants were on breast-milk with crackers added; one had had nothing but breast-milk for three weeks preceding onset — a point at variance with Schrack's opinion (see Morse[1]) that the acetone bodies are not excreted with a pure milk diet. There is evidence that no frozen milk had been used and that no unusual food, such as ensilage, had been given to the cattle.

A few children had eaten unwisely just before the onset of symptoms. One child of 6, for example, went to a party the day before her symptoms began. One of 3 was taken ill four days after eating a large Thanksgiving dinner. One of 5 ate canned shrimp the day before his illness began. One of 3 had pork pie two days before, while in a girl of 5 the parents attributed the attack to mince pie. These indiscretions lose their significance, however, when we find that in nine-tenths of the cases there had been no modification of diet previous to onset.

In only two instances was there evidence of abnormal fat consumption; while, on the contrary, several children were affected who, in order to prevent acidosis, had been most carefully fed on a carbohydrate diet. Thus a boy of 3 was taken ill who, for five days, had eaten only bread, gruels, toast, potato and milk. A boy of 7 for a week had had no solid food and no fats — simply gruels, broths and milk. A girl of 3, on account of a preceding tonsillitis, had been on a liquid diet with low fats and low proteids.

It seems probable that we cannot attribute so extensive an epidemic, if one may use the term, to the milk- or water-supplies, to starvation, to undue fat intake, or to any other dietary error.

The statement that a neurotic temperament plays a prominent part in the etiology of acidosis received scant substantiation. Not more than a fourth of the children were neurotic. In twenty-one the presence of adenoids was noted. Six children had both adenoids and enlarged tonsils, a point worthy of mention because we have found that the removal of adenoids and tonsils, in the intermittent type of acidosis, may be coincident with recovery.

In three instances the illness was ushered in by a bronchial asthma, beginning about twelve hours before the symptoms of intoxication

1. Morse: Arch. Pediat., 1905, xxii, 561.

Four children had follicular tonsillitis immediately preceding. Two had pneumonia, but both pneumonias came late — aftermaths as it were; and in several cases complicated with otitis media the same sequence was observed. Sixty-four children had either a coryza, a bronchitis or both. Occasionally, these two infections were concurrent with the acidosis; more often the infections preceded by three, four, five days or even a week. All told, then, in about 70 per cent. of these cases there was a well-defined infection of the respiratory tract or of its adjacent cavities. If we except one acute nephritis developing ten days after onset, no other types of infection were noted — no instances of complicating appendicitis, for example. In the remaining 30 per cent. — and this group includes two fatal cases — I can put my finger on no suggestive etiologic point.

Many of our patients were too young to attend school; some had apparently come in contact with no other children before they were taken ill. On various occasions two or more children in one house were sick at the same time; but, on the other hand, children were exempted who had been in intimate contact with affected children.

The epidemic was one of first attacks; eighty-four patients were ill of acidosis for the first time. Eleven cases were recurrent. One child had had as many as twenty attacks in eight years. We found that these recurrent attacks were more easily relieved than initial ones, as though a child, in time, acquired a low-grade immunity.

Almost invariably — eighty-six times — the onset was sudden. Prodromal symptoms were the symptoms of a preceding cold or coryza or none at all. Such premonitory derangements as anorexia, listlessness, headache and dizziness were unusual. Three times diarrhea preceded vomiting. Four times the two came together; but as a rule, vomiting came first and was the symptom denoting that a child was ill.

The commoner signs and symptoms enumerated in the text-books, with the number of cases out of a hundred in which they were observed, may well be tabulated:

Signs and Symptoms	No. Cases
Coated tongue	92
Flushed face	74
Drowsiness	64
Thirst	79
Marked prostration	41
Wasting	26
Cerebral symptoms	18
Nervousness or activity	22
Air-hunger	25
Cyanosis	16
Mouth pallor	23
Retracted abdomen	6
Enlarged liver	3
Clay-colored stools	7
Icterus	4
Diarrhea	35

The disease was seen in all degrees of severity. Mild cases yielded very quickly to treatment. Severe cases were pernicious in their activity. Fatal cases were malignant. The average duration of the fatal cases was thirty-two hours, the two extremes being sixteen hours in a baby 14 months old and sixty hours in a child of 5 years.

The more severe the attack the greater was the prostration and wasting, the more evident the meningeal symptoms. So great was the loss of fat in fatal cases that children, in a relatively few hours, shriveled from plumpness to emaciation. With sunken eyes, hollow cheeks and tight-drawn skin they looked not unlike patients in the late stages of phthisis. In such crises delirium and convulsions were expected; twice the clinical picture suggested meningitis.

A coated tongue, a flushed face, drowsiness and thirst were frequent during the active stage of illness. The type of air-hunger peculiar to the disease occurred without cyanosis, but cyanosis did not occur without air-hunger. Rarely a child's face showed complete pallor. Mouth pallor did not occur unless the face was flushed, but, on the other hand, many flushed faces showed no mouth pallor. Retraction of the abdomen was observed only in the more severe and protracted cases, no more frequently, as Griffith[2] says, than would occur in any asthenic state with empty intestines. Abdominal pain was infrequent, as was enlargement of the liver. Icterus, with clay-colored stools, was not nearly so common as other accounts would lead one to anticipate. One child exhibited a punctate red rash on the second day of disease. Otherwise skin lesions and pruritus (noted by Marcy[3]) were lacking.

In few more than a third of these cases was diarrhea observed. Here we had, characteristically, frequent, watery movements, barely colored, containing mucus and occasional fecal particles. A few stools were dark green, two or three were dark chocolate. Blood was almost never present. Normal or constipated stools, which prevailed in two-thirds of the cases, were brown, yellow or black. Watery stools had little odor: those that were solid or semi-solid were usually foul, and in all but one case in which the reaction was tested it was strongly acid. I cannot verify the statement that such stools show an excess of indican (Howland and Richards[4]).

In seven cases vomiting was absent. Normally, it was a predominant feature; food first, changing quickly to watery, mucous fluid, either colorless or yellow, like thin pea-soup. Vomiting was propul-

2. Griffith: Am. Jour. Med. Sc., 1900, cxx, 553.
3. Marcy: Internat. Clin., 1900, iii, 127.
4. Howland and Richards: Arch. Pediat., 1907, xxiv, 401.

sive, frequent and copious. Blood was never present in the vomitus, but in eight instances there were considerable amounts of bile.

Temperature charts showed wide variations. Sixty-five patients exceeded 100 F., and temperatures of 103 or 104 were not uncommon; 105 was reached but once. Generally speaking, high temperatures were observed when there was delirium and marked prostration. On the other hand, of the fatal cases three ranged about 101, one about 100 and one about 99.4. Even subnormal temperatures were not unheard-of. The pulse was invariably elevated, averaging, with a low temperature, from 100 to 120. In children with high temperatures the rate ran as high as 160. There was no evidence of irregularity in the pulse—which heretofore has been described as a common symptom.

Another favorite phrase in the literature is "scanty turbid urine of high specific gravity." In this series we found:

Clear urine	91	
Turbid urine	9	
Amount scanty	50	
Albumin	0	
Sugar	1	(for two days)
Specific gravity (recorded in twenty-seven cases):		
1.010 to 1.015	4	
1.015 to 1.020	4	
1.020 to 1.025	10	
1.025 to 1.030	7	
Above 1.030	2	
Reaction invariably acid.		

Considerable amounts of acetone were present in the urine in every case. Although exceptionally acetone did not appear in the urine until several hours after onset, in ninety-two cases it was found at the first test — practically at the beginning of acute symptoms — which leads to the belief that acidosis of this type is not a sequel of the persistent vomiting and starvation. Acetonuria almost never ceased while a urine was still acid; it tended, rather, to persist for several days after a urine became alkaline, especially if the diet was scanty, but in such an event a patient showed no toxic symptoms. During this period, however, if the urine was allowed to revert into its former acid condition, toxic symptoms were apt to recur. Acetonuria was of little moment, then, if one could procure alkalinity of the urine.

In examining for acetone, we used, commonly, the somewhat inaccurate nitroprussid test. The Lieben method seemed more delicate, while Rothera's test[5] is said to act in a dilution of 1 to 130,000 (Piper[6]). Folin[7] has stated that a large amount of acetone can be present in urine without giving a reaction (Piper[6]). A fruity odor in the breath, attributed to acetone, was noticed in a fourth of the cases. In several

6. Piper: Lancet, London, 1913, ii, 535.
5. Rothera: Australian Med. Jour., October, 1910.
7. Folin: Jour. Am. Med. Assn., 1907, xlix, 128.

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analyses acetone was isolated in the stools and vomitus but only in minute traces.

In only forty-five individuals was the test for diacetic acid made. Fifteen of these were positive with ferric chlorid, but I believe that others would have yielded a positive reaction had specimens been tested more frequently and immediately after they were passed. We found:

Two fatal cases negative.

Three fatal cases positive.

Nine severe cases positive.

Three moderately severe cases positive.

The appearance of diacetic acid presumably indicated failing powers of oxidation. In an acid urine diacetic acid was a danger signal, and as recovery progressed it disappeared from the urine before acetone did.

Oxybutyric acid was found but once. A single analysis for nitrogen and ammonia gave: nitrogen, 10 gm.; ammonia, 0.33 gm.—quantities not far from normal. This child had, however, been under alkaline treatment, which would tend to decrease the absolute and relative excretion of ammonia (Beddard[8]).

We are told in the literature that recovery from acidosis with auto-intoxication is very rapid — as rapid as is the onset. This proved true in sixty cases. If we add our nine deaths we still have an appreciable number of patients that recovered slowly, requiring several days. One child died during this convalescence, apparently from exhaustion.

In this series, treatment comprised the administration of alkalies by mouth or by rectum, catharsis, rectal irrigations and the regulation of diet. Eighty-nine children were given sodium bicarbonate by mouth. Eighty successfully retained it. Three could not retain it; three retained it in part; three refused the solution. Soda was retained well in all but one of the fatal cases, although persistence of vomiting was expected until several doses had been given. The stomach proved tolerant of large amounts of soda.

Certain children preferred the dry salt; they deposited a teaspoonful on the tongue and washed it down with a swallow of water. Nevertheless, concentrated solutions tended to irritate the stomach and cause a recurrence of vomiting; and by concentrated solution I mean one stronger than 1:20: a dram of soda to 2½ ounces of water. This ratio and the ratios 1:32 and 1:60 never caused nausea. Children who received a dram of the salt each hour or two acquired an alkaline urine in from twenty-four to thirty-six hours; those who received a

8. Beddard: Clin. Jour., 1912-13, xl, 65.

dram every four hours, in divided doses, acquired alkalinity in from forty-eight to sixty hours.

Irrespective of age, then, if soda is used, I believe that it is proper to make a solution in the ratio of 1 : 20. Of this solution half an ounce may be given every twenty minutes. No definite rule will fit every case, of course. One must often vary the dilution and the frequency of administration, but he should give the drug freely and in as concentrated a form as is well borne. Edsall's[9] minimum dosage — 100 grains of the bicarbonate — given as rapidly as possible, is much less than was used for many of our cases. The same may be said of Rachford's[10] suggestion that 8 or 10 grains be given every two or three hours and of Koplik's small dosage.[11]

In fatal cases the progress of the disease was so rapid that it seemed impossible to give sufficient alkali — perhaps because "the alkalies are not of much value unless the supply of base to neutralize the acids has failed. If the cause is toxic . . . alkalies are unlikely to do good" (Cautley[12]).

Water proved the most satisfactory solvent for soda. Attempts to disguise the flavor of the salt with orange-juice or grape-juice were usually unnecessary. Of the two, orange-juice was preferable.

Sodium bicarbonate was given by rectum in thirty-two instances: half a dram of the salt in 2 ounces of water injected every hour or two. It was retained in eighteen. A saturated solution given by the drop method at the rate of a drop per second could be continued from twelve to twenty-four hours. It was useless to employ either method if a child had diarrhea.

Potassium citrate and sodium citrate were the alkalies of second choice, used both in conjunction with the bicarbonate and alone, either throughout the illness or during convalescence. One or the other citrate was given to fifty-two children. The citrates proved quite as palatable as the bicarbonate of sodium and were effective in procuring alkalinity. Some children could retain them who could not retain the bicarbonate; the reverse was occasionally true.

Citrates may be given to the amount of half a dram or a dram every hour, in a concentrated solution: 1 ounce of salt to 4 of water. So given, one procures an alkaline urine in less than twenty-four hours, and with these drugs alone one may conquer an acidosis with auto-

9. Edsall: Brit. Med. Jour., 1910, ii, 1033; Am. Jour. Med. Sc., 1903, cxxv, 629.
10. Rachford: Diseases of Children, New York, 1912, pp. 251 and 565.
11. Koplik: Diseases of Infancy and Childhood, New York, 1910, pp. 33 and 505.
12. Cautley: The Diseases of Infants and Children, London, 1910, 149.

intoxication. The administration of any alkali should be continued for a few days after the subsidence of acute symptoms.

It was difficult to ward off an impending attack with any of these drugs. One child of 3 was given, as a preventive, 2 drams of the bicarbonate daily for four days before onset. Another child of 3 received for two days 4 drams of the bicarbonate daily, and for three days 3 drams of sodium citrate daily. So with three or four other cases.

In one fatal case dextrose (a 10 per cent. solution, 2 drams every three hours) was administered by rectum, but was not retained.

Once the vomiting had ceased, most of the children were placed on a simple diet low in fats. Beginning with such liquids as skimmed milk (with or without lime-water), rice-water, barley-water, oatmeal-water, orange-juice, grape-juice, we quickly added malted milk, cereals, crackers, toast, gruels and broths.

Lenhart[13] believes that butter should be excluded, but not other fats. Koplik[11] reduces milk to a minimum. Langstein and Meyer (see Morse[1]) have stated that a fatty diet is dangerous for children when there is disturbance of carbohydrate metabolism. Morse,[1] however, found that the variety of food seemed not to be a salient factor, although in some diseases, especially typhoid fever, in which the acetone bodies appear late, their presence was due to insufficient food or carbohydrates. To my mind, too great stress has been placed on providing a fat-free diet.

Other drugs we used symptomatically. Morphin was occasionally needed to control excitement. Saline solution was sometimes given by rectum. With sundry forms of medication that have been recommended I have had no experience. Let me enumerate a few:

1. Subcutaneous or intravenous injections of dextrose or levulose dissolved up to 10 per cent. strength in normal salt solution (Vander Hoof[14]).

2. Intravenous injection of salt solution (Fischl[15]).

3. Administration of glucose by mouth. Chalfant[16] says this is unsatisfactory. Mellanby[17] advises the administration of glucose rather than the attempt to "neutralize a series of acids, already fully neutralized and of no more significance than creatin."

4. Stomach lavage (Comby[18]).

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13. Lenhart: Cleveland Med. Jour., 1911, x, 1017.
14. Vander Hoof: Charlotte Med. Jour., 1910, lxii, 257.
15. Fischl: Pfaundler and Schlossmann's Diseases of Children, 1912, iii, 171.
16. Chalfant: Jour. Am. Med. Assn., 1912, lix, 852.
17. Mellanby: Lancet, London, 1911, ii, 8.
18. Comby: Arch. de méd. d. enf., 1909, xii, 721.

5. Subcutaneous injection of sodium bicarbonate. Rachford[10] advises 5 or 10 grains to the ounce. Experimentally, this has not proved serviceable (Rhamy[19]).

6. The administration of a mixture of sodium bicarbonate and lithium carbonate (Koplik[11]).

7. Venesection. Withdrawal of 500 c.c. of blood. Introduction of 500 c.c. normal saline solution with 10 gm. of sodium bicarbonate (Houda[20]). This may cause thrombosis (Marchand[21]).

8. Administration of pancreatin (Piper[6] in operative cases).

REPORT OF CASE

Let me give a brief history of a severe case, typical of what we saw in this epidemic:

Patient.—A well-developed, phlegmatic boy, 2 years old, had had duodenal indigestion several times, but recently had been active, vigorous and in good health. He had had no previous attacks of acidosis. His diet had been well regulated with low fats. One other child lived in the same house, but otherwise the boy had not been intimately associated with children. For three or four days he had had a coryza and mild bronchitis.

Sudden onset occurred with vomiting at 5 a. m. The child continued to vomit at frequent intervals, especially if anything — even a little water — was taken by mouth. The vomitus became pale, watery and slightly yellow. With the aid of an enema he evacuated a semisolid brown stool—foul, slimy, acid. There was no diarrhea.

The temperature gradually rose to 103.5 F.; the pulse increased from 90 to 140. The boy's face was flushed with a contrasting whiteness about the mouth and nose. His breath came quickly, eagerly. One minute he was restless and uneasy, crying out for his mother, the next relapsing into stupor. In his waking moments he asked for water.

Examination. An examination made under difficulties showed coryza, a furred tongue, a retracted neck, pupils that were dilated but reacted to light, a slightly distended abdomen — nothing else. The urine was clear, strongly acid, with a specific gravity of 1.025, free from albumin and sugar. Acetone and diacetic acid were present. The white count was elevated but not remarkable.

Treatment was difficult and without material effect. As the hours passed the symptoms became more intense, the child's abdomen was noticeably retracted, his eyes sunken, his body wasted. Finally, toward midnight he had a convulsion and in a few minutes was dead.

In this particular case the necropsy, twelve hours post mortem, gave the following data:

Pathologic Examination (Macroscopic).—Body of a well-developed, well-nourished, white male child. Pupils equal, dilated.

Primary incision shows skin thin, abdominal fat very slight; muscle firm, normal color, non-bleeding.

Peritoneal cavity: Very little fat in omentum. Superficial veins of intestines not remarkable. Intestinal mucosa normal except for conspicuous glands. Stomach mucosa injected.

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19. Rhamy: Jour. Am. Med. Assn., 1912, lviii, 628.
20. Houda: Jour. Am. Med. Assn., 1912, lviii, 1194.
21. Marchand: München. med. Wchnschr., 1912, lix, No. 4.

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Liver 10 cm. below costal margin and 10 cm. below xiphoid. Extends upward to cartilage of fifth rib. Prominent areas, size of a bean, white in color, on anterior surface. Gray in spots on section.

Adrenals, pancreas and kidneys normal.

Brain: Adhesion of dura to pia in region of closed posterior fontanelle. Vessels prominent and congested. Surface of brain moist but without excessive fluid.

Pathologic Examination (Microscopic).—Liver: Fatty metamorphosis, edema, hemosiderin pigmentation.

Spleen: Acute hyperplasia.

Pancreas: Post-mortem degeneration.

Thymus: Atrophy. Necrosis and calcification of corpuscles of Hassal.

Stomach: Normal.

Appendix: Follicular hyperplasia.

Diagnosis: Fatty degeneration of the liver; congestion of the brain.

Cultures from the several organs were negative except one from the base of the brain. Here we cultivated two kinds of cocci. One was unusually large and occurred in pairs; its colonies were white. The other coccus was as large as staphylococcus; its colonies were translucent.

Antigen was made from the mixture, and from the larger coccus and from a culture of meningococcus. All of these gave a negative test with blood-serum from a second case of acidosis with auto-intoxication. We cannot rule out the possibility that the immune bodies which fix the complement had not yet developed in this serum.

By blood-culture we obtained from this latter case a coccus which was not identical with either of the cultures procured at autopsy. Numerous cultures made from throats and nasal discharges in other cases gave variegated growths from which no specific organism could be isolated.

GENERAL DISCUSSION

Acidosis has been defined as an "abnormal metabolism of carbon leading to the appearance of organic acids in the blood and urine, and the formation of ammonia to neutralize these acids" (Cautley[12]).

These organic acids, beta-oxybutyric and diacetic, with acetone, comprise the acetone bodies. It is said that oxybutyric acid is the precursor of diacetic acid and acetone the final product of the series; yet there is no good reason for so believing, except the order of their appearance in the urine, the similarity of their chemical formulas and the fact that diacetic acid, when heated, changes to acetone. Against this view is the fact that acetone can readily be formed from a number of other substances. Furthermore, the administration of sodium aceto-acetate is followed by the elimination of beta-oxybutyric, just the reverse of the common understanding of their order of formation (Rhamy[19]).

When the total amount of acetone bodies formed is low, the percentage of acetone itself is high; when the total amount of acetone bodies is high, the percentage of acetone itself is low (Piper,[6] in post-operative cases). If the excretion of acetone exceeds 0.5 gm. daily diacetic acid is present also. If the excretion of acetone exceeds 1 gm. daily, beta-oxybutyric acid is present (Beddard[8]).

Koplik[11] has stated that acetone arises from the splitting of nitrogenous substances of the body. Von Noorden,[22] however, says that though tissue destruction is a necessary factor, there is no evidence that acetone comes from the breaking down of proteids. It is readily obtained from fats and has been obtained from carbohydrates (Brackett[23]). Knoop[24] has demonstrated the formation of acetone bodies from fatty acids. By feeding 100 gm. of oleic acid to a healthy man, Joslin (see Brackett, Stone and Low[23]) caused an excretion of over 1,700 gm. of acetone in twenty-four hours, without producing other symptoms. Geelmuyden noticed acetonuria after adding olive oil and butter to a normal diet (Rhamy[19]).

The processes by which fat is burned are dependent on the simultaneous combustion of carbohydrates. The acetone bodies are probably excreted as a result of a lessened oxidation of fat, brought about either indirectly as a result of lessened sugar combustion, or by a direct influence of some unknown nature on fat combustion (Howland and Richards[4]). This direct influence, according to Guthrie,[25] is an intoxication produced by absorption of toxins from the intestines, by bacterial poisons — for example, pneumonia — or by inorganic poisons — for example, phosphorus. The liver, already laden with fat, becomes surcharged with more fat derived from the subcutaneous tissues. Should the overtaxed liver fail to metabolize the enormous quantity of fat thus brought to it, the circulation becomes flooded with the products of imperfect oxidation.

Brackett[23] states that although the presence of primary intestinal toxins has not been shown, it is probable that they exist, while Mellanby[17] suggests that such toxins arise directly at the portal area from intestinal infection or putrefaction.

The acetone bodies constantly appear in some lesions of the pancreas, which fact, too, is in accord with the intestinal origin of some cases of acid intoxication, since disturbance of pancreatic function would reduce digestive activity in the duodenum with resulting faulty cleavage of fats (Rhamy[19]).

We know that acetone is found in very small amounts in the urine of healthy children (Baginsky[26]), never exceeding 1 cg. in twenty-four hours (Langstein and Meyer). Indeed, acetone and its associates, diacetic and oxybutyric acids, are possibly being constantly formed in minute quantities in normal metabolism (Rhamy[19]).

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22. Von Noorden: Clinical Treatises on Metabolism. New York, 1903.
23. Brackett, Stone and Low: Boston Med. and Surg. Jour., 1904, cli, 2.
24. Knoop: Ztschr. f. d. gesammte Biochemie, 1905, vi, 150.
25. Guthrie: Brit. Med. Jour., 1908, ii, 1158.
26. Baginsky: Arch. f. Kinderh., 1888, ix, 1.

In increasing amounts they are formed in many pathologic conditions: in starvation and cachexia; in eclampsia; in poisoning by phosphorus, salicylates and by other drugs; in hepatic lesions like acute yellow atrophy; in diabetes; in nervous disturbances due to fright; in the so-called delayed anesthetic poisoning. Sedgwick[27] and Smith[28] have called attention to the frequency with which their formation accompanies adenoids. Comby[18] remarks that 50 per cent. of his series had appendicitis and believes that this is an etiologic factor that has been overlooked by other observers. Harris[29] notes their occurrence in scarlet fever. Gordon[30] (quoting Reiche) states that acetonuria was present in 60 per cent. of a series of thirty-two hundred diphtheria cases. Frew[31] examined 662 out-patient children of whom 61.6 per cent. showed acetonuria. These were largely infectious cases and the nature of the concomitant infection seemed not to affect this ratio; except that in typhoid fever only 15.6 per cent. of the children showed acetonuria. Chalfant[16] obtained positive results in 86.45 per cent. of his cases, affected with postoperative vomiting.

Morse[1] states that acetone bodies are present in the urine of infants and children under approximately the same conditions as in adults. They are often present in acute diseases accompanied by high fever (especially in the acute exanthems, diphtheria and pneumonia), vary, as a rule, directly with the height of the fever and disappear with the fall of the temperature. Morse has noted, also, the enormous increase of these bodies in children during convulsions, but thinks they are not the cause of the convulsions. Acetone bodies are rarely found in the urine in gastro-intestinal disorders of infancy but are commonly found during childhood, whether the disorders are acute or chronic. There may be no accompanying symptoms of acid intoxication.

In these instances, although a state of acidosis exists, with the acetone bodies present in the blood, the hydrogen ions are "rapidly neutralized by sodium in the tissue fluids, potassium in the cells, and by alkaline earths chiefly derived from bones. If this is not enough, the excess is neutralized by ammonia, derived from protein, which would normally have been metabolized into urea" (Cautley[12]). There is a consequent increase in the excretion of ammonia and a diminution in urea (Rhamy[19]). In children it is invariably true that acidosis in the body is accompanied by an increase in the excretion of ammonia (Langstein and Meyer).

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27. Sedgwick: Am. Jour. Dis. Child., 1912, iii, 209.
28. Smith: Lancet, London, 1911, ii, 1186.
29. Harris: Lancet, London, 1910, i, 1346.
30. Gordon: New York Med. Jour., 1913, xcvii, 529.
31. Frew: Lancet, London, 1911, ii, 1264.

"Should more acid be produced than can be thus neutralized, the reaction of the tissue fluids may be altered and cause symptoms of acid intoxication. It is therefore evident that acidosis may be very common, though acid intoxication is rare. It can exist long before the tissue fluids are rendered less alkaline and before toxic symptoms arise. One passes gradually into the other (Cautley[12])."

It is said that acetone is non-toxic; it is argued that in "recurrent vomiting" acidosis can be prevented by the administration of dextrose and yet the acute symptoms occur just the same (Beddard[8]). Edsall[9] has said that acetone and diacetic acid have little if any significance in producing symptoms, for neither is very toxic; that beta-oxybutyric acid, however, is more important and produces the only form of auto-intoxication. According to Piper,[6] the acetone bodies, when excreted freely, are harmless. Injected intraperitoneally and subcutaneously into guinea-pigs, large amounts of acetone gave no anatomic lesions unless the administration was prolonged for many days (Brackett[23]).

Despite the fact that the acetone bodies are only mildly toxic, the general conception is that oxybutyric and diacetic acids, by uniting with the fixed alkalies, reduce the alkalinity of the tissues and thereby produce a condition of toxemia. The amounts of these two acids are in constant relation and with acetone vary directly as the severity of the intoxication (Edsall[9]). The ammonia excretion is perhaps another index of the degree of intoxication, although Ewing[32] found that in pregnancy the estimation of ammonia nitrogen did not follow this rule.

With the neutralization of the alkalies of the tissues, the blood can carry less carbon dioxid; there may be a decrease from the normal 24 per cent. to 3 per cent. Hence, carbon dioxid accumulates in the tissues until we have a condition of internal suffocation (Vander Hoof[14]).

At variance with this theory is Lenhart's[13] view that while the blood is less alkaline to titration, this fact does not prevent it from carrying carbon dioxid. Venous blood will take up carbon dioxid and in acid intoxication the carbon dioxid of the tissues is not excessive. The carbon dioxid is an incident. Benedict,[33] too, while admitting that the alkalinity of the tissues cannot be inferred from that of the blood, has stated that in conditions other than diabetes the alkalinity of the blood may be lower than that ever observed in diabetic coma, without the appearance of the symptoms of intoxication.

Rachford[10] has suggested that the acids, besides removing alkaline bases which are needed in metabolism, have a direct toxic action in that they bring poisonous alkaline bases (as ammonia) into the blood. Ewing,[32] too, from his experimental work, has concluded that the intoxication may be due to the accumulating antecedents of urea. He

32. Ewing: Arch. Int. Med., 1908, ii, 330.
33. Benedict: Arch. f. d. ges. Physiol., 1906, cxv, 106.

adds that none of the principles of the theory of acid intoxication have been proved — namely, carbon dioxid asphyxiation, degeneration of the vital organs by withdrawal of alkalies and reduced alkalinity.

Partial reports of a dozen or more necropsies in children are available. In these the predominating lesion was enlargement and fatty infiltration of the liver. Other data were:

LANGMEAD,[34] CASE 1.—Kidneys fatty. No nephritis. Mucous membrane of posterior wall of stomach mottled by dark red areas of hemorrhage.

LANGMEAD, CASE 2.—No organism could be grown from the blood, spleen or bile. Nine c.c. of blood yielded 0.33 per cent. acetone.

LANGMEAD, CASE 3.—Three c.c. of blood yielded 0.24 per cent. acetone.

GRIFFITH.[2]—Necrotic changes in mucous membrane of stomach and intestine; slight parenchymatous alterations in pancreas, spleen and kidneys.

BRACKETT[23] (FOUR NECROPSIES).—Only marked lesion was extreme fatty degeneration of liver and muscles.

ABT.[35]—Fatty degeneration of all the organs.

Rhamy[19] believes it is probable that there are essential changes in the blood-vessels, brain and excretory organs, ending in acute degeneration of the liver. Crile's[36] experiments would lead one to anticipate, also, changes in the adrenals.

Rosenfeld (see Langmead[34]) showed that if animals were fattened on mutton-fat and then poisoned with phloridzin, acute fatty infiltration of the liver occurred and that the fat so deposited was mutton-fat. From this Langmead concludes that the liver condition is a result, not a cause. Brackett[23] thinks the adipose tissue of the body furnishes the fat in the liver.

There is evidence, then, that the acetone bodies are derived from fatty acids imperfectly metabolized in the liver; that this imperfect metabolism may be coincident with lessened sugar combustion; but that there is an immediate exciting cause for this imperfect metabolism.

Sometimes an intestinal disturbance is the only obvious exciting cause, and here we have the "digestive" type of acidosis. Again, we have primary poisoning from an inorganic poison, while in a third group one must consider a concomitant infection. In the "infectious" type, however, there may be intestinal disturbance, evidenced by diarrhea, foul stools and the like. The increased excretion of ammonia may be due not only to the incomplete metabolism of urea, but to the entrance through the portal circulation of a bacteriologic product accruing from putrefaction in the large intestine (Folin and Denis[37]).

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34. Langmead: Brit. Med. Jour., 1907, ii, 819; 1905, i, 350.

35. Abt: Am. Jour. Med. Sc., 1914, cxlvii, 86; Jour. Am. Med. Assn., 1910, lv, 991 (discussion).

36. Crile: Personal communication.

37. Folin and Denis: Jour. Biol. Chem., 1912, xi, 161.

In the Concord epidemic one saw acidosis with auto-intoxication in all degrees of severity; one saw both initial and recurrent cases. I believe that "acid auto-intoxication," "recurrent vomiting" and "cyclic vomiting" are merely degrees of an acidosis. The beneficial effects of alkaline treatment suggest that the symptoms are due to an excess of acid. In spite of the fact that the acetone bodies formed are apparently less in amount than those found in diabetes, their constant presence suggests, further, as Morse[1] has said, that they have an intimate relation with the symptoms; that they comprise, in fact, the acids causing this hyperacidity.

The Concord epidemic bore an analogy to the Birmingham epidemic reported by Parke.[38] It differed in that the Birmingham cases had an initial diarrhea, constant enlargement of the liver, absence of cyanosis and not infrequently absence of vomiting. Parke reported eighteen cases in infants under 20 months with an alarming death-rate (71 per cent.). It is also of interest that the symptoms in our epidemic were not unlike those attributed in several localities last year to the consumption of blighted chestnuts.

To the best of my knowledge an extensive epidemic similar to that in Concord has not heretofore been reported. With so few bacteriologic data I can offer slight evidence that any organism was the immediate exciting cause. Nevertheless, I believe that the prevailing respiratory infection was significant; that this infection was usually conveyed by direct contact; that it was selective and that some infected children did not develop acidosis.

My thanks are due to the several physicians whose cases are included in this compilation and to various officials at the Harvard Medical School who examined the bacteriologic and pathologic specimens.

38. Parke: Jour. Am. Med. Assn., 1910, lv, 991; 1907, xlix, 1827.

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A RESPIRATION INCUBATOR FOR THE STUDY OF THE ENERGY METABOLISM OF INFANTS*

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For the study of the metabolism of infants, especially new-born or premature infants, it is important to have perfect control of the temperature to which the child is exposed. Preliminary work on animals with a respiration chamber surrounded by water, the latter kept warm by means of a gas-flame placed underneath, convinced me that a more exact control was necessary before observations on the infant could be undertaken. In casting about for a satisfactory type of thermoregulator, the Freas oven came to mind and after conference with the inventor (Prof. Thomas B. Freas, Dept. of Chemistry, Columbia University) as to the feasibility of the application of his regulator to the purposes in hand, plans were agreed on for the construction of an electric incubator which would be suitable for the introduction of a respiration chamber large enough to contain an infant one year of age. Dr. Freas has placed the laboratory under special obligations for the interest he has shown in the execution of these plans.

This particular incubator measures 60 by 82 by 115 cm. outside and 46 by 48 by 100 cm. inside. It rests on a special iron stand provided with it, 85 cm. above the floor and makes a good appearance as a piece of laboratory or hospital furniture (Figs. 1 and 2).

The regular plan of construction of the Freas air thermostat[1] was departed from in only a few particulars. For example, it was necessary to have a considerable number of openings through the wall for the passage of the ventilating-pipes and cooling-coil, the introduction of thermometers, the connection of the oxygen regulator, etc. The range of temperature was fixed at from 20 to 50 C., the capacity of the heater being limited to 200 watts. The motor for driving the stirring-fan (Fig. 5, *F*) which is provided with the incubator was mounted on a large steel spring so that the vibrations should be damped out to some extent. The glass doors were made as large as the front

* From the Physiological Laboratory of the Cornell University Medical College, New York City.

1. Freas, Thomas Bruce: A Study of Thermostats, Dissertation, University of Chicago, 1911.

end, thus permitting plenty of light to enter and were provided with strips of felt so as to make the closure practically air-tight.

THE RESPIRATION CHAMBER

The chamber measures 30 by 32 by 76 cm. inside. It was made of 14-ounce tinned copper, strongly lock-jointed and soldered, and was rimmed at the front end by a heavy brass casting. Another casting of the same dimensions was made as a frame for the glass head or door of the chamber. The glass is held in place by litharge cement covered with heavy wax and a coat of white-lead. A heavy rubber gasket is

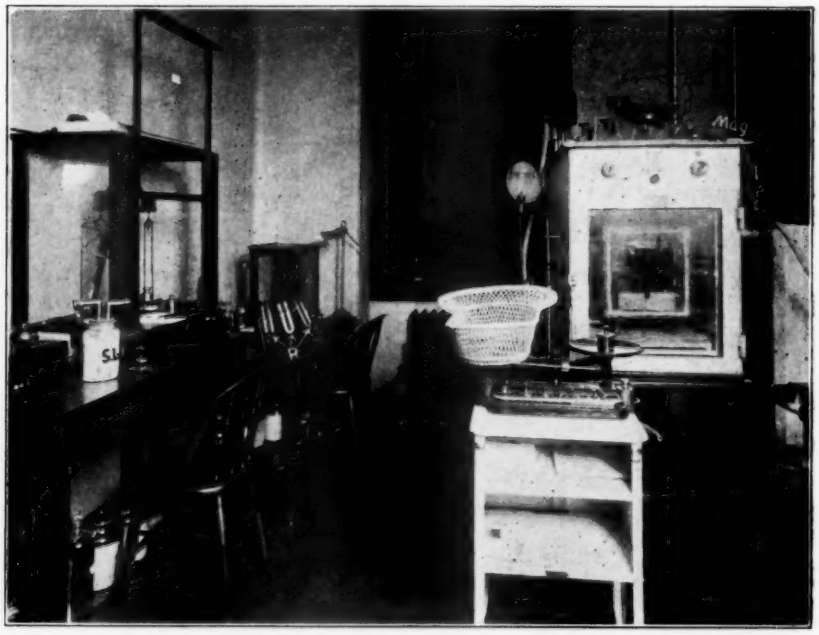

Fig. 1.—General view of room in Bellevue Hospital containing respiration incubator (Eimer and Amend) set up ready for use. The inner chamber is shown through the glass doors of the incubator. Inside the chamber the bed is seen. The balances on the left of the room are used in weighing the absorbers. The balance in the middle of the room (sensitive to 1 gm.) is used in weighing the infant. Further description in the text.

cemented to the brass rim, and a perfectly air-tight closure of the chamber is secured by clamping the frame of the head firmly against this gasket by means of twelve L-shaped steel bolts, which engage the back side of the brass rim (Figs. 2 and 3). The chamber is mounted on wooden runners and is strongly reinforced by means of three galvanized iron ribs girthing it at equal intervals from front to back.

Pressure changes inside or outside the chamber, therefore, do not alter its volume.

Since the incubator measures 46 by 48 by 100 cm. inside, a space 7.5 cm. wide is left on all sides of the chamber. The air in this space is kept in motion by a fan (Figs. 4 and 5).

VENTILATION AND MEASUREMENT OF RESPIRATORY EXCHANGE

The ventilation of the respiration chamber is accomplished by means of a Benedict "universal respiration apparatus,"[2] connected to it by means of wide rubber tubing and ½-inch brass pipes. The brass pipes are screwed into strong brass bushings soldered to the copper

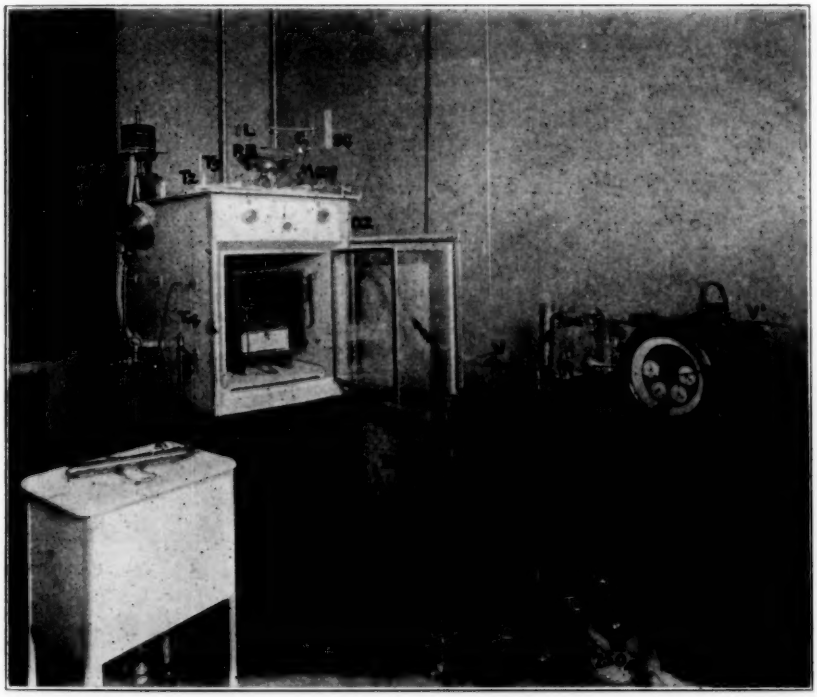

Fig. 2.—Another view of the same room. The absorber table is seen at the right. The glass doors are open and the glass head of the inner chamber is lying on the shelf below the incubator. The stethoscope tubes may be seen lying on the nurse's table and the bell of the stethoscope inside the incubator. Further description in the text.

wall. The inlet pipe enters at the upper back corner of the chamber on the right side and the outlet is connected with the lower front corner on the left. Thermometers are admitted to the inlet and outlet pipes by means of T joints (Fig. 3, *T*4). The arrows in Figure 2 show the direction of the air current.

2. Benedict, F. G.: Am. Jour. Physiol., 1909, xxiv, p. 345; Deutsch. Arch. f. klin. Med., 1912, cvii, 156; Am. Jour. Dis. Child., 1914, viii, 1.

The Absorber System.—The Benedict apparatus was so constructed for use with the incubator that by turning valves (V and V', Fig. 2) the absorbers could be quickly changed after stopping the blower, without the loss of more than 20 c.c. of air.† Each set of absorbers consists of two soda-lime jars for absorption of carbon dioxid and a sulphuric acid absorber for catching the water lost from the soda-lime. Each of these absorbers is small enough to be weighed (separately) on a Sartorius balance sensitive to 0.001 gm. The soda-lime absorbers are made on the plan (Fig. 1, *S. L.*) adopted for the absorbers used with the Sage calorimeter in Bellevue Hospital.[3] The sulphuric acid

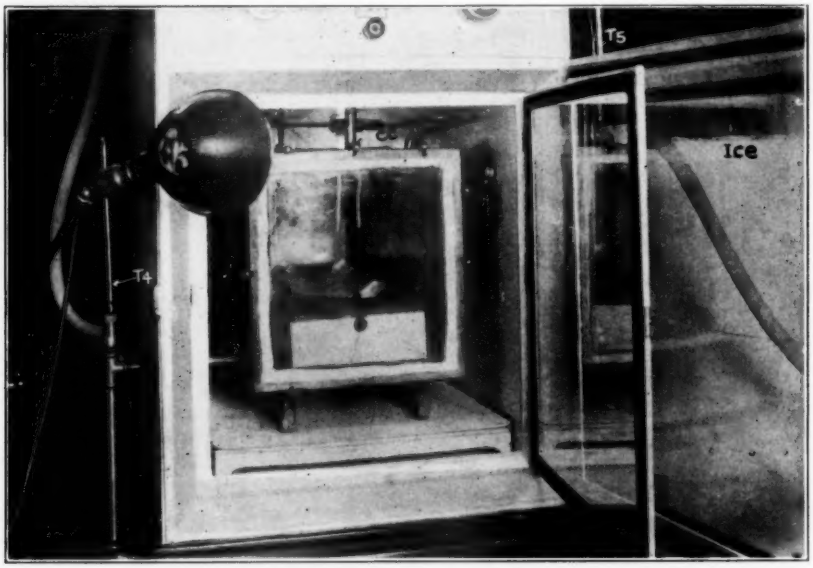

Fig. 3.—A near view of the interior of the incubator showing the cooling coil, *c.c.*

absorber is the gas washing-bottle designed by Williams[4] for use with the animal calorimeter in this laboratory. Immediately following the sulphuric acid absorber is a brass tower containing sponges kept moist with very dilute sodium hydroxid solution, which serves the double purpose of imparting a slight amount of moisture to the air and of arresting any traces of acid fumes which may come from the drying-bottle.

Since the water given off from the lungs of the child does not enter into the computation of the heat production by the indirect method

† Since this was written the table has been reconstructed so two sets of absorbers can be connected at once and the change from one to the other accomplished with a single lever operating both valves.

3. Lusk, Soderstrom and Riche: Arch. Int. Med., to appear soon.

4. Williams: Jour. Biol. Chem., 1912, xii, 323.

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(except as this water may affect the volume of the oxygen admitted), the absorbers used in the collection of this water are not weighed. They consist of two Williams bottles placed in series after the blower on the under part of the absorber table (Fig. 2, H_2SO_4). A brass trap (Fig. 2, *Tr.*), of a capacity about equal to the amount of the sulphuric acid contained in the first Williams bottle, is introduced for the safety of the blower. A bicycle coaster brake on the large pulley of the blower makes it impossible to turn the blower the wrong way; but the trap would catch any acid which might be drawn back by sudden blockade of the air-circuit at any point.

The Residual System.—The measurement of the oxygen absorbed by the child is based on the general proposition that oxygen be admitted to the air-circuit just as rapidly as it is used. This presupposes that the respiratory products should be absorbed and removed from the air as rapidly as they are produced. The efficiency of the absorbers is such that as far as the welfare of the child is concerned the ventilation is perfect. Neither carbon dioxid nor water vapor can accumulate to any appreciable extent. But an *absolutely* perfect adjustment of the rate of ventilation so as to leave the composition of the air *exactly* the same at the end of a period as at the beginning is impossible, especially if the child should cry or void urine near the end of the period. Since the admission of oxygen is regulated by the total volume of the air, (see below) and since this volume will vary with the amount of water vapor in it as well as with the temperature and barometric pressure, it is necessary to know the composition of the air at the close as well as at the beginning of a period. The analysis is carried out by diverting a measured sample of air from the main circuit, causing it to flow through a special set of absorbers and returning it to the system without loss of anything more than the small quantities of carbon dioxid and water contained in it. These analyses are called the residuals because they give information as to the amounts of the various gases residual in the air at definite moments.

A small copper pipe is tapped into the main circuit on the positive side of the blower (Fig. 2, *R*) and is led upward through the top of the table. By turning a stop-cock at the base of this pipe a small fraction of the total air current can be drawn off. The residual absorbers consisting of three U tubes (Fig. 1, *R*) (the first containing sulphuric acid and pumice stone, the second finely granular soda-lime and the third sulphuric acid and pumice stone again)[5] are connected to this small pipe and the air having passed through them is conveyed to the meter (Fig. 2, M) where it is measured, thence through a drying-

5. Cf. Benedict and Carpenter: Carnegie Institution of Washington, Publ. 123, p. 73.

tower[6] (the meter contains water) and back to a point (Fig. 2, x) in the main system where the pressure is low.

The U tubes are weighed to the fourth decimal place before and after drawing off the sample. When the amounts of water vapor and carbon dioxid in this measured sample (usually 5 liters) are known, the total amounts in the entire system are readily calculated. By a series of corrections which will be better understood after the method of conducting an alcohol check is explained, the amount of oxygen residual in the air at the time the air sample is taken can also be computed.

The Oxygen System.—Oxygen is admitted into the ingoing air so that it may be thoroughly diffused into the chamber. The amount admitted is regulated by the method first described by Benedict and Carpenter[5] and as slightly modified by Williams[4] in his construction of the animal calorimeter. The essential parts of this arrangement consist of a rubber bag or spirometer which serves as a tension equalizer and volume indicator at the same time (Figs. 1 and 2, *RB*) and a magnet (*Mag.*), which, when actuated, releases pressure on a rubber tube leading from the oxygen cylinder (O_2). The rubber bag communicates with the respiration chamber by means of a brass pipe, and a valve in this pipe permits the bag to be shut off from the chamber. The oxygen cylinder[7] while in use is suspended from a strong hook at the right side of the apparatus conveniently near the magnet. The magnet is connected through a resistance board carrying three lamps and through the mercury cups (*C*), situated on the horizontal arm above the magnet, with the house current. A lever (*L*) 38 cm. long is pivoted above the bag and is so counterpoised that it rests lightly on the bag by means of a broad metal disk. The arm ends at the right in a point which traverses a scale (*Sc*). It carries contact points which dip into the mercury as the lever descends. As the oxygen in the air of the circuit is used up by the child the bag collapses until the lever makes contact with the mercury (sparking is prevented by means of a condenser not shown in the figures). This actuates the magnet and releases pressure on the pure gum tubing leading from the oxygen cylinder. Oxygen thereupon enters the circuit until the volume is increased sufficiently to break the electric circuit, when pressure is again applied to the tubing thereby shutting off the oxygen; and so on.

6. The drying-tower is not shown in the figure because it stands behind the meter.

7. Purchased from the Consolidated Dental Mfg. Co., New York. These cylinders measure 4 cm. diameter by 33 cm. in length. They will contain about 50 gm. of oxygen under a pressure of 100 atmospheres. Together with the reduction valve the cylinder weighs about 1.5 kg. and can be weighed on the Sartorius balance to 0.001 gm.

At the beginning of a period oxygen is let into the system by hand until the pointer of the lever rests at a certain mark on the scale. At the end of the period the system is again filled to exactly the same point. If the volume of the air has not changed (by change of temperature, pressure, or composition of the air) the loss in weight of the cylinder would be the amount of oxygen consumed. Such conditions, however, would be very exceptional; hence all corrections must be made for every period.

Oxygen cannot be let into the system by any such automatic arrangement until the pressure which exists in the cylinder is reduced to a pressure which the rubber tube will withstand. A valve which reduces this pressure to a few pounds per square inch was made for these cylinders by the mechanician of the laboratory, Mr. James Evenden. It is shown in Figure 4.

Switch-Board.—A special switch-board, the end of which can be seen in Figure 6, provides electric outlets for: (1) the heater of the incubator; (2) the fan motor; (3) the motor on the absorber table; (4) the oxygen regulating system, and (5) any extra lamps required for illumination of the balances (Fig. 1), the interior of the incubator (Fig. 3), etc.

The Cooling-System.—The walls of the incubator being constructed of materials having a low coefficient of conductivity, the heat produced by the infant would not be conducted away as rapidly as produced and the temperature inside would rise unless the room air were at a very low temperature. To counteract this tendency and to furnish a chilling effect against which the heater of the incubator should operate, a cooling-system was installed. This consists of a coil (Fig. 3, *cc*) of copper pipe, ¼ inch inside diameter, making several turns on the two sides and the top of the inner wall of the incubator and carrying a stream of tap-water. At ordinary room temperature and with tap-water coming directly from the mains (that is, not warmed unduly by the house pipes) it is not necessary to chill the stream. It flows, however, through a coil of pipe inside an ice-tank (Figs. 1, 2 and 3), and in very warm weather the water can easily be kept down to the desired temperature by placing ice in contact with the coil. To secure a constant flow the water is given a constant head of pressure by passing it through a flush tank, operated by a ball cock, placed near the ceiling of the room. (This tank is too high to be seen in any of the figures, but the pipes leading to and from it are seen.) After passing through the cooling-system the water is conducted back to the sink.

A thermometer (Figs. 1 and 3, *T*5) is placed in the stream of water, and a wheel valve is placed near the tank, so that the cooling effect can be regulated to some extent both by the amount of ice and

by the rate of flow of the water. The thermoregulator of the incubator takes care of the finer regulation. The heater is sufficient to keep the space about the respiration chamber at 27 C., even when the water is at 4 C. and the rate of flow 400 to 600 c.c. per minute. This would be wasteful of electric current, however, and a water temperature of from 10 to 15 C. with a rate of 200 to 300 c.c. of water is more than sufficient to carry away the heat produced by a year-old infant even in very warm weather, unless the infant cries actively. In the latter case the speed of the water can be increased, or more ice can be introduced or

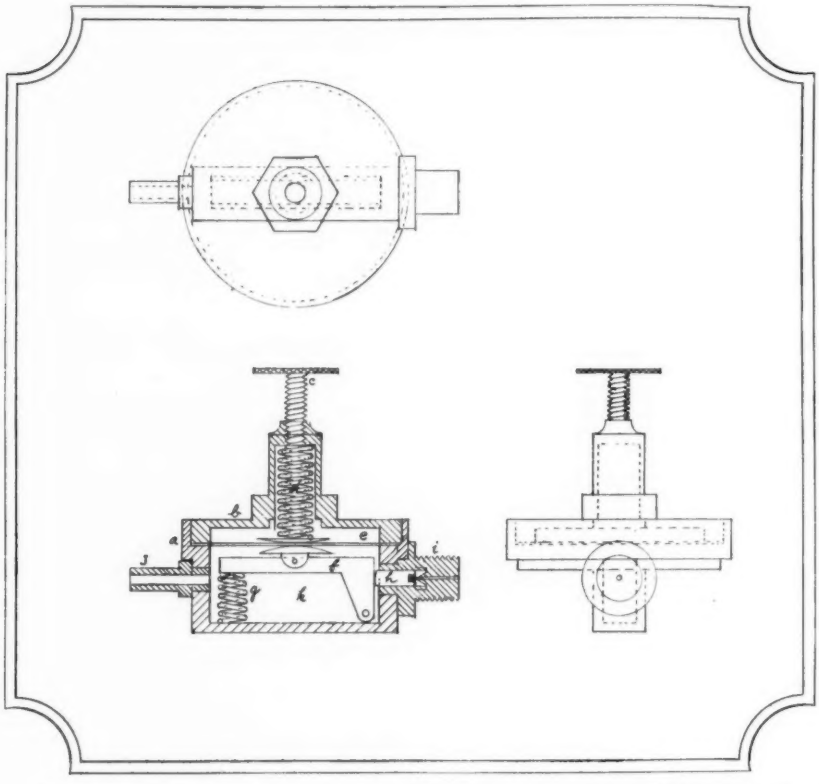

Fig. 4.—Detail of reducing valve used on small oxygen cylinder: *A*, case; *B*, lid of case; *C*, screw to compress spring; *D*, spring to reduce diaphragm; *E*, diaphragm; *F*, lever to close valve; *G*, spring to raise lever; *H*, valve with hard rubber tip to control oxygen; *I*, end to screw into oxygen cylinder; *J*, end for hose, oxygen supply. Oxygen contained in cylinder is held back by valve *H*. By compressing spring *D* with screw *C* lever *F* is lowered, thus allowing valve to come back and permitting oxygen to enter chamber *K* until the pressure beneath the diaphragm is sufficient to bring it to its original position which shuts off the oxygen again. When the oxygen in chamber *K* is below the desired pressure the tension of spring *D* again lowers the lever and repeats the operation.

the heater can be turned off. With such a cooling effect as just mentioned the temperature outside the chamber falls very quickly, and within a very few minutes also the temperature inside the chamber.

HEAT CONTROLS

Many control tests were made with the incubator as adapted in this way to the purposes of a respiration apparatus, both empty and with animals, before it was used with infants. Four thermometers are regularly used in the following positions: No. 1 (not shown in

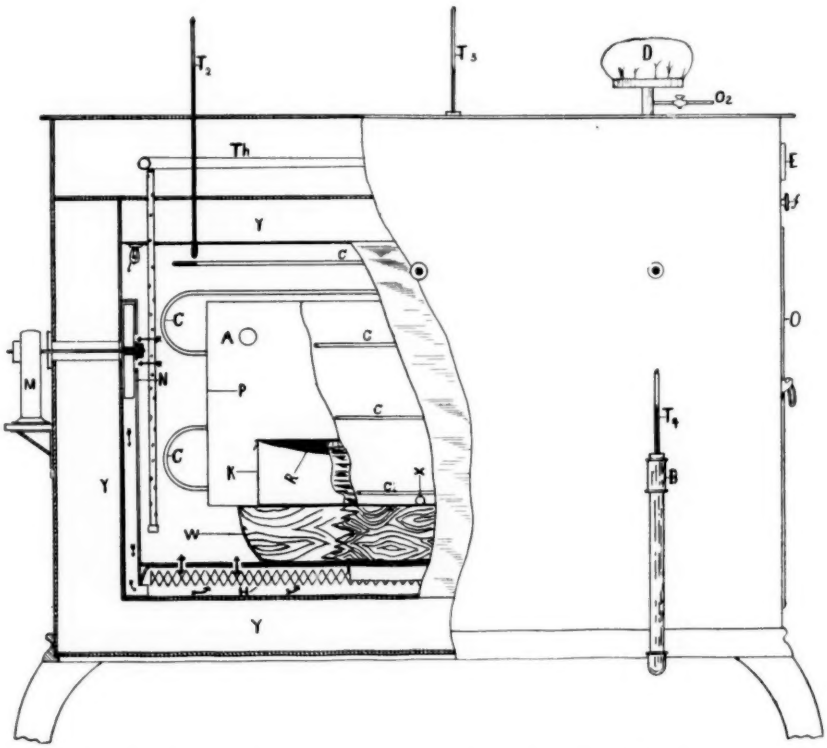

Fig. 5.—Sectional view of the incubator from the side. *Y*, asbestos packed wall; *H*, heater coil; *C*, cooling pipes; *P*, copper wall of inner chamber; *A*, point of entrance for air; *B*, exit pipe for air, containing thermometer; *W*, wooden runner which supports copper chamber; *K*, bed inside respiration chamber; *R*, rubber diaphragm; *Th*, thermo regulator; *M*, fan motor; *N*, fan. Arrows show direction of currents which equalize temperature inside the incubator. *D*, rubber bag for regulation of oxygen; *l*, lamp; *f*, control for setting regulator at any desired temperature.

any illustration) in the ingoing air; No. 2 on the top at the rear end of the incubator, the bulb extending into the outer air space; No. 3 (T_3, Figs. 1, 2 and 5) on top near the center, the bulb extending 1 inch

into the inner air-space, and No. 4 in the outgoing air. All these thermometers are graduated to tenths of a degree C. and can be read to 0.05°. An air thermometer is usually kept on the wall near the absorber table.

Table 1 will serve as an example of the accuracy of the heat control. The subject was a small black dog, 4 kg. in weight, which lay perfectly still the entire hour.

TABLE 1.—HEAT CONTROL SUBJECT, SMALL BLACK DOG

	Temperature			
Time P. M.	Thermometer No. 1 Ingoing Air Degrees	Thermometer No. 2 Between Walls Degrees	Thermometer No. 3 Inner Chamber Near Center Degrees	Thermometer No. 4 Outgoing Air Degrees
1:50	23.0	27.0	28.1	27.9
1:55	23.1	27.2	28.1	28.0
2:00	23.1	27.2	28.1	28.1
2:05	23.2	27.3	28.1	28.1
2:10	23.3	27.2	28.1	28.1
2:15	23.4	27.2	28.15	28.1
2:20	23.5	27.1	28.15	28.1
2:25	23.5	27.15	28.15	28.1
2:30	23.5	27.15	28.15	28.1
2:35	23.5	27.1	28.1	28.15
2:40	23.5	27.2	28.1	28.1
2:45	23.6	27.0	28.1	28.1
2:50	23.6	27.0	28.1	28.1

The air temperature rose 0.6 of a degree during this observation and the temperature in the outer air space fluctuated somewhat according as the heat happened to be on or off at the moment of reading; but the temperature inside the inner chamber hardly varied at all during the entire hour.

CONTROL BY COMBUSTION OF ALCOHOL

The accuracy of the entire respiration apparatus has been checked many times in the course of the year and a half during which it has been in use, by combustion of alcohol in the chamber and the determination of the "respiratory quotient" of the flame. In the great majority of these check experiments all corrections have been made; but at times it has been sufficient to measure the oxygen by loss in weight of the cylinder with a correction for argon and the carbon dioxid by gain in weight of the absorbers without further corrections. With the flame burning uniformly the carbon dioxid residual in the circuit often does not change at all from the beginning to the end of a period. The water almost always falls the first period and then remains constant.

An example of a complete check experiment is given showing the manner of making all corrections. The same corrections and the same methods of calculation are used when the subject is a child.

Dec. 23, 1913. Alcohol check experiment.
Contents of respiration chamber — alcohol lamp and bed.

Vol. of air containing CO_2 67 l.
Vol. of air containing H_2O 66 l.
Vol. of air containing O_2 and N_2 69 l.

First period from 4:52 to 5:52 p. m.

At 4:52 residual analysis.

5 liters air contain 0.0178 gm. CO_2 and 0.0136 gm. H_2O
67 liters air contain 0.238 gm. CO_2 (=0.121 l.)
66 liters air contain 0.179 gm. H_2O (=0.223 l.)

To find residual O_2.

Temperature 28.06 C.; barometer 765.1 mm.

log. 69 = 83885 0.121 l. CO_2 + 0.223 l. H_2O = 0.344 l.

$$\log. \frac{1}{1 + .00367(28.06)} = 95740$$

$$\log. \frac{765.1}{760} = 00290$$

79915 = 62.973 l. at 0° and 760 mm.
0.344 l. CO_2 and H_2O

62.629 l. O_2 and N_2

Subtracting four-fifths for N_2 50.1032

12.5258 l. O_2

At 5:52 residual analysis.

5 liters air contain 0.0178 gm. CO_2 and .0136 gm. H_2O
67 liters air contain 0.238 gm. CO_2 (0.121 l.)
66 liters air contain 0.129 gm. H_2O (0.223 l.)

To find residual O_2.

Temperature 28.23 C.; barometer 765.3 mm.

log. 69 = 83885

$$\log. \frac{1}{1 + .00367(28.23)} = 95719$$

$$\log. \frac{765.3}{760} = 00302$$

79906 = 62.960 l. at 0° and 760 mm.
.344 l. CO_2 and H_2O

62.616 l. O_2 + N

Subtracting N with which exp'm't started, 50.1032

12.5128 l. O_2

"Respiratory Exchange" Period 1

Gain in weight of CO_2 absorbers 4.850 gm.
Loss in weight of O_2 cylinder... 5.090 gm.
0.6 % correction for argon = 0.03 gm.

Loss in weight due to oxygen = 5.060 gm.

Residual analyses show: (1) no change in CO_2 of air but (2) amount of O_2 is less. (12.5258 — 12.5128 = .0130 l. = .0186 gm.) This shows that flame

used a little more O_2 than was admitted; therefore, 5.060 + .0186 = 5.079 gm. O_2 actually used. Reducing weights to volume:

log. weight CO_2 (4.850 gm.) = 68574
log. weight to vol. (CO_2) 70680

39254 = 2.469 l.

log. weight O_2 (5.079) = 70578
log. weight vol. (O_2) = 84496

55074 = 3.554 l.

$$\text{R. Q.} = \frac{\text{Vol. } CO_2}{\text{Vol. } O_2} = \frac{2.469}{3.554} = .695$$

Second period from 5:52 to 6:52.
At 6:52 residual analysis.

5 liters air contain 0.0166 gm. CO_2 and .0114 gm. H_2O
67 liters air contain 0.222 gm. CO_2 (=0.113 l.)
66 liters air contain 0.150 gm. H_2O (=0.187 l.)
0.113 + 0.187 = 0.300 l. CO_2 and H_2O.

Temperature 28.4 C. Barometer 765.3 mm.

$$\log. 69 = 83885$$

$$\log. \frac{1}{1 + 00367(28.4°)} = 95695$$

$$\log. \frac{765.3}{760} = 00302$$

79882 = 62.924 l. at 0° and 760 mm.
0.300 l. CO_2 and H_2O

62.624 l. O_2 and N
Subtracting N_2 with which exp'm't started 50.1032

12.5208 l. O_2

"Respiratory Exchange" second period.
Gain in weight of CO_2 absorbers 4.968 gm.
Residual analyses show that CO_2 in air was less at 6.52 than at 5.52 (0.238 — 0.222 = .016) 4.968 gm.
.016

Actual amount of CO_2 given off = 4.952 gm. = (2.521 l.)

Loss in weight of O_2 cylinder..... 5.500 gm.
Less 0.6 per cent. for argon..... .033

5.467 gm.

Residual analyses show more O_2 in air at 6.52 than at 5.52
12.5208 — 12.5128 = .0180 l. = .026 gm.

5.467
.026

Actual amount of O_2 used by flame = 5.441 gm. = (3.807 l.)

$$\text{R. Q.} = \frac{2.521}{3.807} = .662$$

First period.. .695
Second period .662

Average ... .677 Theory .666; error 1.6 per cent.

Table 2 gives the respiratory quotients obtained with the alcohol lamp for all the experiments between June 1, 1913, and July 1, 1914, on which all corrections could be made:

TABLE 2.—RESPIRATORY QUOTIENTS FOR EXPERIMENTS BETWEEN JUNE 1, 1913, AND JULY 1, 1914

Date	Quotient	Date	Quotient	Date	Quotient	Date	Quotient
6/ 5/13	0.654	1/ 5/14	0.652	1/20/14	0.664	2/ 9/14	0.684
	0.675	1/ 8/14	0.642		0.656		0.644
	0.655		0.628				0.641
			0.667	Average...	0.660		
Average...	0.661					Average...	0.656
		Average...	0.646				
7/30/13	0.669	1/11/14	0.661	2/ 3/14	0.656	3/ 4/14	0.645
	0.670		0.671		0.653		0.637
					0.644		
Average...	0.669	Average...	0.666			Average...	0.641
				Average...	0.651		
12/ 1/13	0.617	1/16/14	0.741	2/ 5/14	0.673	6/24/14	0.627
	0.724		0.610		0.631		0.666
			0.638		0.644		
Average...	0.670					Average...	0.642
12/23/13 ...	0.695	Average...	0.663	Average...	0.649	7/29/14	0.652
	0.662						
Average...	0.677						

It will be seen that a perfectly theoretical result not infrequently occurs in a single period, but that often one period shows a high and the succeeding one a low result, the mean being very near to the theoretical value. This in most instances is due to a rise or fall of temperature near the end of the first period. The average error for all of the daily averages is 1.8 per cent.

CONTROLS WITH DIABETIC DOGS

Dogs completely under the influence of phlorhizin or deprived of the pancreas have a total incapacity to oxidize glucose. This results in a respiratory quotient[8] which varies but slightly from 0.69. The diabetic dog, therefore, is a suitable subject for controlling the efficiency of a respiration apparatus of this type. The apparatus here described has been used in the study of certain problems in connection with pancreatic diabetes.[9] The following are examples of the quotients obtained on dogs which were known from the relation of dextrose to nitrogen in the urine to be completely diabetic:

Dog VI.	July	9, 1913.	R. Q.	11.27-12.27	.68
				12.27- 1.27	.68
Dog C.	July	23, 1914.	R. Q.	3.42- 4.27	.69
				4.27- 5.13	.68
				8.03- 8.49	.68
Dog E.	Aug.	4, 1914.	R. Q.	5.27- 6.27	.683
				8.27- 9.27	.685

8. With the depancreatized dog this level is not invariably reached until about the fourth or fifth day after operation.. Cf. Verzár: Biochem. Ztschr., 1914, xlxvi, 75.

9. Murlin, Edelmann and Kramer: Jour. Biol. Chem., 1913, xvi, 79 and Kramer and Murlin; ibid., 1914.

Animal experiments of this kind furnish a better control of the efficiency of the apparatus for work with infants than does the alcohol flame, for the reason that both the chemical and the physical properties of the air are more nearly like those of an experiment with the child. As a matter of course, the entire air circuit is thoroughly sterilized by means of formaldehyd, circulated by means of the blower, before the apparatus is used with the infant.

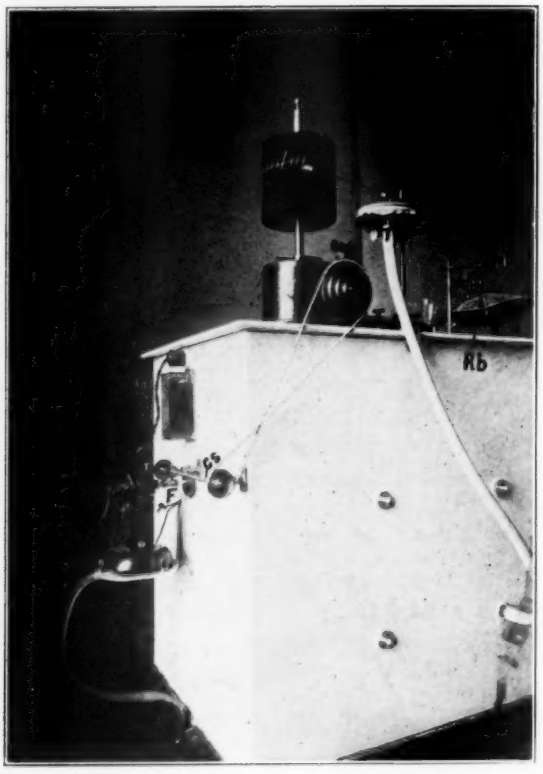

Fig. 6.—View of the rear end of the incubator showing fan motor (*F*); counter shaft (*CS*) for driving kymograph, and large recording tambour (*T*) for registering movements of the infant. *Rb*, rubber bag for equalizing tension and regulating flow of oxygen into the circuit.

OXYGEN BLANK

This form of control, introduced by Williams,[10] has been found useful as a check on the gas analysis. It consists in sealing up the chamber, starting the blower and taking off a sample of air just as in starting a period for an alcohol check, but without a subject or lamp in the chamber. If the air which is thus closed in the circuit is some-

10. Williams: Jour. Biol. Chem., 1912, xii, 346.

what moist, the water absorbers will remove the water and its place will be taken by oxygen from the cylinder. The same would happen if the temperature were permitted to fall. At the end of an hour another sample of air is taken for analysis, and after the corrections for temperature and pressure are made, the amount of water lost from the air, as indicated by the residual analyses, should be equal to the amount of oxygen which has been lost from the cylinder. In such a check conducted on June 22, 1914, the amount of oxygen admitted was 0.346 liter in one hour. The air lost 0.411 liter of water; the carbon dioxid did not change. The temperature had risen 0.2° and

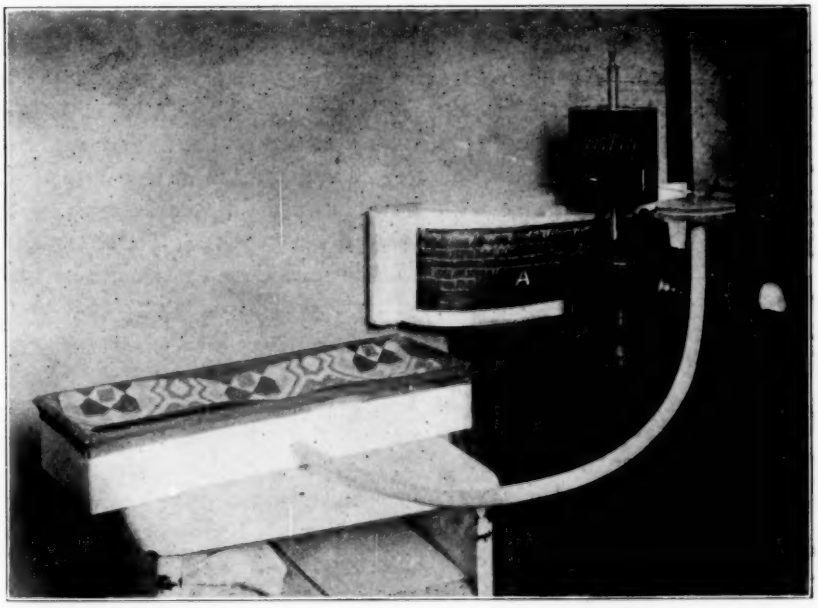

Fig. 7.—Rubber bed used for recording motions of the child, showing the wide tube and large tambour necessary for quick transmission. The character of the tracings obtained is seen in the open book (A).

the barometer had remained stationary. The temperature change caused an expansion of 0.056 liter in the entire system which would serve to keep out that much oxygen. Hence (0.346 + .056 =) .402 l. of oxygen, with no temperature change, would have been admitted to replace a (calculated) shinkage of 0.411 liter.

REGISTRATION OF MUSCULAR ACTIVITY OF INFANT

The fan motor can be utilized for driving a kymograph situated on top of the incubator (Fig. 6). A small counter-shaft (*cs*) driven by a worm gear working on the axle of the fan carries a small pulley at

its outer end and this connects directly with the driving pulley of the kymograph.

For recording the actual motions of the infant several devices have been employed.[11] One of them employed with new-born infants consists of two large tambours connected by wide rubber tubing (Fig. 7). One of these tambours is the infant's bed while in the respiration chamber. The other (6 inches in diameter) carries a lever which writes directly on the smoked paper.

The bed consists of a galvanized iron box (10 by 22 by 61 cm.) covered with a piece of rubber sheeting. The rim of the box over which the sheeting fits is so made that the rubber comes in contact successively with two surfaces, each about 1 cm. broad, before it reaches the outside surface of the box itself. The corners, of course, are all rounded. An air-tight joint was secured by means of thick alcohol shellac. After the joint had been coated heavily with the shellac, the box was left for some days inverted on the rubber surface and weighted. Then the second surface was treated in the same way and the rubber tied firmly with a heavy cord. After several days' drying it was found to be air-tight. As a receiving plate for the infant's body a piece of linoleum of appropriate size was cemented to the upper surface of the rubber sheeting. A light blanket placed over this made a very comfortable bed.

Every motion of the infant was transmitted as an air wave to the recording tambour. In fact, the only objection to the device was its extreme sensitiveness. Even the pulsations of the air caused by the ventilating blower were recorded (Fig. 7 A). With older infants[12] the bed was discarded and the muscular motions were recorded by means of a cuff on the leg and a very flexible pneumograph placed about the chest.

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11. See following papers.
12. See paper by Murlin and Hoobler to appear in this journal shortly.

INTRAVENOUS INJECTION OF DIPHTHERIA ANTITOXIN IN CHILDREN*

EDWIN HENRY SCHORER, M.D.
KANSAS CITY, MO.

The benefits of the antitoxin treatment of diphtheria are well recognized. From 1878 to 1894 in New York City the deaths from diphtheria per hundred thousand of population ranged from 110 to 264 and from 1890 to 1895 the combined diphtheria deaths in the larger European and American cities from 66.9 to 80.4 per hundred thousand population, while following the general use of diphtheria antitoxin since 1895 the deaths per hundred thousand of population have varied in New York City between 22 and 91, and between 19 and 55.6 in the larger cities of the world.

Diphtheria antitoxin was first used generally in 1895 and in 1896 first manifested its real value in the United States. Gradually fewer deaths from diphtheria have occurred, but it must be evident that in the past few years the death-rate has not been decreased materially. That we still have some deaths due to the disease is too well known. When deaths occur in patients having received antitoxin we generally believe them due to one of three causes: late administration of antitoxin, injection of insufficient amount of antitoxin, or the presence of exceptionally virulent diphtheria bacilli. Knowledge of these facts, however, is of little value in some of the cases of diphtheria seen, for any one having charge of diphtheria patients in a hospital for contagious diseases or doing consultation work in the diseases of children meets with patients who have had diphtheria for some days, but have had little or no diphtheria antitoxin administered. No wonder, then, that the need for further investigation of the treatment of diphtheria should be recognized and that any method which enables diphtheria antitoxin to exert its influence at the earliest possible time after adminsitration should be tried.

We know that it is through the blood that antitoxin is distributed to the places where it binds toxins, and last year Park[1] reported from his experiments that he believed 5,000 units introduced intravenously are as beneficial as 20,000 units injected subcutaneously. His experiments showed that six hours after injection the blood-serum contains twenty units per cubic centimeter of blood when injected intravenously

* Received for publication Nov. 10, 1914.

1. Park: Boston Med. and Surg. Jour., 1913, clxviii, 73.

and two when given subcutaneously, and after twenty-four hours twelve units when given intravenously and six when injected subcutaneously.

Intravenous injection of diphtheria antitoxin was long ago practiced, but has usually not been followed because the subcutaneous method gives good results and intravenous injection is difficult in children. The veins of the arm are often too small, so in this series antitoxin was administered by way of the external jugular vein. Martha Wollstein[2] reported obtaining blood for cultures from children

TABLE 1.—GENERAL RESULTS OF DIPHTHERIA ANTITOXIN INJECTIONS

	Subcutaneous Injection		Intravenous Injection	
		Average		Average
Day of disease on which injections were made..	3, 8, 10, 3, 8, 7, 5	6.3	1, 3, 2, 2, 3, 2, 6, 10, 3, 3, 3, 10, 7, 3	4.1
Units injected at one time	3,000 × 2 5,000 × 7	4.555	5,000 × 10 10,000 × 6	6.875
Number of injections made	9	1.3	16	1.1
Days after injection on which fever and membrane were absent and patients felt well.....	13, 6, 4, 5, 10	7.6	2, 1, 3, 2, 1, 2, 1, 2, 4, 2, 2, 3	2.1
Days after injection on which diphtheria bacilli were absent	30, 36, 43, 16, 8	26.6	12, 8, 14, 2, 8, 2, 5, 5, 4, 6, 4, 6	5.4
Total days sick.....	15, 20, 12, 15, 15	15.4	3, 4, 5, 4, 4, 4, 7, 12, 14, 5, 5, 10	6.4
Total days confined.....	31, 44, 38, 22, 37	34.4	18, 20, 22, 11, 16, 14, 11, 23, 26, 7, 16, 13	16.4
Carriers	.....	4.	.....	0.
Serum reactions	.....	0.	.....	4.
Immediate reactions.....	0		4	
Deaths	.....	2.	.....	2.
Laryngeal diphtheria....	.....	2.	.....	7.
Paralysis ..... { Cardiac	.....	3.	.....	0.
Paralysis ..... { Palatine	.....	1.	.....	1.

by going into the jugular vein and the method she suggested was employed in the cases reported here. In all, fourteen children received intravenous injections of diphtheria antitoxin. The results and symptoms observed are compared with those obtained in the same epidemic by subcutaneous injection in seven cases. The latter patients were seen in consultation and some had received diphtheria antitoxin before they were seen by me. The general results are shown in Table 1.

2. Wollstein, Martha, and Morgan, Edward: Blood Cultures During Life in Infants and Young Children, with Description of a New Technic, AM. JOUR. DIS. CHILD., October, 1912, p. 197.

It is evident that so small a series does not offer enough evidence on all of the facts detailed. It seems fair, however, to draw some conclusions from the data. It will be observed that following intravenous injections the fever and membrane disappeared sooner and the patients felt well; that diphtheria bacilli disappeared more rapidly; that there were fewer carriers and that paralyses were less frequent than when subcutaneous injections were made.

Two children died in each series; death occurred from seven to fourteen hours after the first injection in each case. All four children who died had laryngeal diphtheria, but there were seven cases of laryngeal diphtheria in the series that received intravenous injections, and only two in the series given subcutaneous injections.

Reactions, however, followed only intravenous injections. The data in regard to this are shown in Table 2. These reactions are classified as "immediate" and "serum" reactions.

TABLE 2.—Intravenous Injection Reactions

Immediate Reaction		Average	Serum Reaction		Average
Time after serum injection	1, 1, 1½, ½ hrs.	1 hour	Days after serum injection	9, 10, 10, 6	8.8
Temperature elevation	103.2, 104 103.8, 103.2	.....	Rash	.....	4 cases
Disappeared in...	3 hrs., 20 hrs. 5 hrs., 20 hrs.	12 hours	Glandular enlargement	.....	1 case
Respiratory distress	2 cases	.....	Articular pain..	.....	1 case
			Days on which symptoms disappeared	2, 2, 2, 3, 1	2.25

"Immediate Reaction."—Generally, the introduction of diphtheria antitoxin is not believed to be followed by an elevation of temperature, but slight elevations do occur frequently. When given intravenously, four injections out of sixteen were followed in from one-half to one and a half hours by striking symptoms. These were usually ushered in by a marked chill, then an elevation of temperature from 103.2 to 104 F., and in two cases by respiratory distress. All of these symptoms disappeared in from three to twenty hours, when the patients usually felt entirely well. That these were serum reactions did not seem to be the case, as in none did the later serum rashes appear. When serum rashes and reactions did occur they did not differ from those following other serum injections, though none occurred in the small series of patients receiving subcutaneous injections.

SUMMARY

It is not to be inferred that intravenous injections are advocated in all cases, but intravenous injections undoubtedly produce results more rapidly and so are to be preferred in late and severe cases.

Intravenous injection is less painful at the time of administration and later, and because of the smaller number of units necessary intravenous injection is much less expensive. Entrance into the jugular vein in children is not difficult and this vessel affords a ready site for the intravenous injection of diphtheria antitoxin when the median basilic and the cephalic veins are too small. This small series indicates that there are fewer carriers and heart failures are less likely to occur following intravenous injection, but there are more immediate and serum reactions. The immediate reactions never impressed us as being grave and in themselves did not seem to be a contra-indication to intravenous injection of diphtheria antitoxin.

Rialto Building.

THE SUGAR-CONTENT OF THE BLOOD IN CHILDHOOD *

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In the last few years our knowledge concerning sugar in the circulating blood has made considerable advances.[1] The keen interest aroused by the questions concerned with glycemia has led to the perfection of numerous methods which in turn have resulted in greater numbers of cases being studied. The importance of the study of the blood-sugar is well emphasized by Scott,[2] who says:

> Glycemia offers a more satisfactory indication of the condition of mobile sugar than does glycosuria; first because either an increase or a decrease in the amount of sugar may be demonstrated, while normal urine can show only an increase; secondly, because profound changes in glycemia may occur in response to conditions which do not produce glycosuria; thirdly the blood is in much more direct relation to the living cells than is the urine.

Though the variety of methods used has led to slightly divergent readings, it may be stated that the blood-sugar in the normal adult is about 0.09 per cent., varying from 0.06 to 0.12 per cent., and remains remarkably constant between these limits. Anything above 0.12 per cent. should be considered hyperglycemia. Such increase above the normal in the blood sugar has been found after taking food — the so-called alimentary hyperglycemia. As examples of this, Bing and Jacobsen,[3] who consider 0.13 the highest normal level for the fasting adult, found that after taking 100 gm. of sugar by mouth the percentage in the blood rose to about 0.2 after one to two hours. Goetzky[4] also found that the blood-sugar reached its maximum one-half hour after eating and then gradually descended to reach normal level again about three hours later. Though all investigators are not in absolute agreement as to these data, nevertheless these are important points,

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* Received for publication Oct. 10, 1914.

* From the Laboratory of Physiological Chemistry of Cornell Medical School; the Pediatric Dispensary of Mount Sinai Hospital, and the Sanitarium for Hebrew Children at Rockaway Park.

1. Retzlaff, Karl: Neuere Arbeiten über den Blutzucker, Med. Klin., 1914, Nos. 19 and 20.

2. Scott, E. L.: Content of Sugar in the Blood under Laboratory Conditions, Am. Jour. Physiol., 1914, xxxiv, 306.

3. Bing, H. J., and Jacobsen, B.: Blutzuckeruntersuchungen unter normalen und einigen pathologischen Verhältnissen, Deutsch. Arch. f. klin., Med., cxiii, 571.

4. Goetzky, F.: Der physiologische Blutzuckergehalt beim Kinde nach der Mikromethode von Bang, Ztschr. f. Kinderh., 1913, ix, No. 1.

for in making any determinations, cognizance of the time of the preceding meal must be taken. Beside alimentary hyperglycemia, an increased blood-sugar is also found under various pathologic conditions, including diabetes, certain cases of nephritis, fever and after hemorrhage.

As far as infants and children are concerned, until relatively recently the sugar content of their blood had not been investigated for the reason that not only were the existing methods extremely cumbersome and tedious, but also too great a quantity of blood was needed for analysis. In the last few years, however, several new methods have been elaborated by which both of these drawbacks are overcome. The micro-method devised by Ivar Bang[5] requiring but a few drops of blood, naturally removed the greatest hindrance to the study of the sugar content of the blood of infants, and as a result we are now in possession of a series of cases in which this question has been studied.

Cobliner,[6] Goetzky,[4] Bing and Windelow[7] and Mogwitz[8] have examined a series of infants and have shown that in general the blood-sugar content is about the same as that of adults (0.07 to 0.11). In starvation the blood-sugar sinks to about half its former value (Mogwitz). Infants also show alimentary hyperglycemia which is more marked after taking sugar than after starch, probably because the latter is more slowly absorbed from the gastro-enteric canal.

The micro-method of Bang, which was the one used in all the determinations on infants and children, aside from the fact that the extremely minute amount of blood used and the resultingly small quantity of sugar actually determined would seem to allow of a large error in the results obtained, is moreover a rather complicated method, requiring much special apparatus. It constitutes, therefore, a scientific and laboratory method rather than a clinical one.

Through the kindness of Professor S. R. Benedict, I was enabled to make use of a method which has been devised by himself and Dr. R. C. Lewis, which not only has the advantage of requiring a relatively small amount of blood (though not so small as the Bang method), but also is one of extreme simplicity. The method depends on the fact that when a sugar solution is heated with a saturated solution of picric acid in the presence of an alkali, a definite colorimetric reaction results, the depth of the color being directly proportional to the quantity of sugar present. The method as used by me is a modification by Lewis

5. Bang, Ivar: Der Blutzucker, Wiesbaden, 1913.
6. Cobliner, S.: Bluthzuckeruntersuchungen bei Sauglingen, Ztschr. f. Kinderh, 1910, i, 207.
7. Bing and Windelow: Blutzuckerbestimmungen bei Kindern, Ztschr. f. Kinderh., 1913, ix, No. 1.
8. Mogwitz: Ueber den Blutzucker der Säuglinge, Monatschr. f. Kinderh., 1913, No. 9.

and Benedict of their method published[9] in 1914. A description of the method in detail follows:

A little more than 2 c.c. of blood is drawn from the vein at the elbow and placed in a small beaker. With an Ostwald pipet, 2 c.c. of the blood is then transferred to a 25 c.c. flask in which has been put 6 c.c. of distilled water. The pipet is rinsed out once with 2 c.c. of distilled water. The flask is then filled to the 25 c.c. mark with a saturated solution of picric acid. The heavy precipitate is now filtered off and a clear yellow filtrate obtained. Eight c.c. of this filtrate is transferred to a 20 cm. Jena glass test-tube, and to this is added 2 c.c. of a saturated solution of picric acid, 1 c.c. 10 per cent. sodium carbonate solution, two drops of petroleum oil (liquid albolene) and four small glass beads. This is then heated just to dryness directly over a Bunsen flame. The beads and the oil prevent the solution from "bumping" and frothing. The residue is redissolved in 5 or 6 c.c. of water and the solution brought to a boil. The mixture is then quantitatively poured into a 10 c.c. flask through a small bit of cotton wool in a funnel in order to remove the oil. The test-tube is washed with a few cubic centimeters of water and this is added to the contents of the flask, which is then cooled to room temperature and filled up to the 10 c.c. mark with water. The solution is then ready to be examined in the colorimeter. Its color is compared with a freshly prepared standard sugar solution, or, better, with a solution of picramic acid.[10]

The calculation of the blood-sugar is made as follows: Originally, 2 c.c. of blood was taken and made up to 25 c.c.; but only 8 c.c. of the filtrate was used; therefore, the sugar actually determined was that in 0.65 c.c. blood. If, as an example, the reading of the unknown solution is 12.0 when 0.00065 gm. sugar solution reads 10.0, we find the amount of blood-sugar present as follows:

$$\frac{10.0}{12.0} \times \frac{1}{10} = 0.083 = \text{the percentage of sugar in the blood.}$$

With this very simple method by which a determination can be made within fifteen minutes, it seemed worth while to examine a series

9. Lewis, R. C., and Benedict, S. R.: A Method for the Estimation of Sugar in Small Quantities of Blood, Proc. Soc. for Exper. Biol. and Med., 1914, xi, 57.

10. The standard solution of picramic acid is made up as follows: 0.065 gm. picramic acid is dissolved in about 25 c.c. water; 0.1 gm. sodium carbonate is added and the solution warmed until all the acid is dissolved. The solution is then made up to 1 liter with distilled water. The color of this solution is permanent and is standardized against a known solution of sugar treated by the method above outlined. It was found that when a sugar solution containing 0.00065 gm. sugar (dextrose) was treated by the method and put in the colorimeter set at 10.0, its color exactly corresponded to the picramic acid solution set at 10.0. The picramic acid solution was therefore used as a standard set at 10.0, at which it was considered to equal 0.00065 mg. sugar.

of bloods obtained from children. In all, sixty children were examined. Of these twenty-six were normal. The remainder, as may be seen from Table 2, were suffering from a variety of complaints. The ages of the children varied from 2 to 14 years. The children were examined from two and one-half to three hours after eating breakfast, so that any postprandial hyperglycemia might be avoided. The temperature in all the cases but one (No. 55) was normal. None of the children showed glycosuria.

TABLE 1.—BLOOD-SUGAR DETERMINATIONS IN TWENTY-SIX NORMAL CHILDREN

Case No.	Age, Years	Sugar, Per Cent.
1	2	0.085
2	3	0.089
3	4	0.084
4	5	0.098
5	6	0.108
6	6	0.092
7	7	0.072
8	7	0.073
9	8	0.100
10	8	0.093
11	8	0.113
12	8	0.085
13	8	0.088
14	9	0.104
15	10	0.093
16	10	0.079
17	10	0.085
18	11	0.098
19	11	0.093
20	11	0.078
21	11	0.108
22	11	0.086
23	12	0.080
24	12	0.084
25	14	0.105
26	14	0.073

In the series of normal children (Table 1) the percentage of sugar varies from 0.072 to 0.113; in other words, it does not vary from the percentage found in adults. The only other series of blood determinations in children above infancy which I was able to find in the literature is that published by Goetzky[4] in 1913. He used Bang's micro-method on one hundred normal infants and children and found the average percentage of sugar in the blood of thirty-three children between the ages of 2 and 12 years to be 0.102, the extremes being 0.087 and 0.118. My own findings are somewhat lower, as may be seen from the following synopsis of Table 1:

Age	Percentage		
2- 5 years.	0.084 to 0.098.	Average 0.089.	Goetzky's findings 0.097.
6- 9 years.	0.072 to 0.113.	Average 0.091.	Goetzky's findings 0.105.
10-14 years.	0.073 to 0.108.	Average 0.087.	Goetzky's findings 0.104.

That the age of the child does not seem to influence the sugar content is shown by the fact that the youngest children, from 2 to 5 years old, had an average of 0.089 per cent., those from 6 to 9 years an average of 0.091, and finally, those from 10 to 14 years an average of 0.087 per cent. These results, moreover, do not corroborate Goetzky's finding that the percentage of sugar is slightly higher in older children than in the younger. Sex had no influence on the readings.

TABLE 2.—BLOOD-SUGAR DETERMINATIONS IN VARIOUS ABNORMAL CONDITIONS

No. Case	Years Age	Disease	Per Cent. Blood-Sugar
27	11	Compensated mitral regurgitation.	0.088
28	9	Compensated mitral regurgitation.	0.085
29	9	Compensated mitral regurgitation.	0.091
30	12	Compensated mitral regurgitation.	0.076
31	10	Compensated mitral stenosis.	0.095
32	12	Decompensated mitral regurgitation.	0.068
33	12	Decompensated mitral regurgitation.	0.069
34	12	Decompensated mitral regurgitation.	0.060
35	10	Endocarditis; adherent pericardium.	0.062
36	9	Neurotic.	0.108
37	13	Neurotic.	0.085
38	10	Neurotic.	0.104
39	11	Neurotic.	0.074
40	13	Orthostatic albuminuria.	0.111
41	9	Orthostatic albuminuria.	0.093
42	10	Orthostatic albuminuria.	0.124
43	12	Chronic nephritis.	0.089
44	14	Chronic nephritis.	0.094
45	6	Adenoids.	0.089
46	10	Facial tic.	0.072
47	13	Chorea.	0.117
48	7	Chorea.	0.090
49	6	Chorea.	0.072
50	5	Cyclic vomiting (during attack).	0.104
51	9	Cyclic vomiting (between attacks).	0.082
52	10	Cyclic vomiting (between attacks).	0.096
53	9	Intestinal indigestion.	0.088
54	3	Measles.	0.080
55	4	Malaria (temperature 106.2°).	0.087
56	12	Progressive muscular dystrophy.	0.078
57	11	Tuberculous hip.	0.098
58	6	Tuberculous hip.	0.106
59	7	Tuberculous knee.	0.091
60	9	Convalescent meningitis.	0.080

In Table 2 will be found the readings taken on the blood of children suffering from various ailments. It will be seen that in general there is no great departure from the normal figures. Patients 27 to 35 are children suffering from cardiac complaints of various kinds. Those whose hearts were fully compensated (Nos. 27 to 31) gave normal readings; whereas those showing failure of the circulation gave very low readings (Nos. 32 to 35). Two of these severely ill cases had albuminuria and all four had enlarged livers. The case of endo-

carditis, adherent pericardium and ascites (No. 35) presented considerable cyanosis, but the blood-sugar was low, 0.062, which is unusual since cyanotic cases have been found to show a mild hyperglycemia.

Three cases of orthostatic albuminuria were examined and all three gave high readings. Bing and Jacobsen,[8] who report a blood-sugar determination in a young girl of 16 with this urinary anomaly, found no variation from the normal figure. No conclusions can be drawn from three cases, but the high results are certainly interesting, especially in view of the fact that some cases of nephritis also show a hyperglycemia.

In a case of malaria, the blood examined one hour after the chill, when the temperature was 106.2, showed a normal sugar value.

Of particular interest are the cases of cyclic vomiting. In this condition, in which numerous factors in the urine examination point toward a disturbance of carbohydrate metabolism, a deviation from the normal in the amount of sugar in the blood might be anticipated. As may be seen in the table, however (Nos. 50 to 52), the figures for the blood-sugar are well within the normal limits. Patients 51 and 52 were examined between attacks while in apparently good health, their urine showing no trace of acetone. Patient 50, on the other hand, was seen on the fourth day of a typical attack of cyclic vomiting with marked acetonuria. The child, who had retained nothing, not even much water, looked very pale and appeared considerably prostrated. He was examined at 10 a. m. and had taken nothing by mouth since the evening before, when he had been given some milk which was promptly vomited. The blood-sugar was found to be 0.1040.

The blood-sugar in only one other case of cyclic vomiting has been studied: Hilliger[11] published a case of a 6-year-old girl in whom severe attacks of vomiting with great amounts of acetone in the urine could be brought about at will by withdrawing all the carbohydrate from the diet. At such times the blood-sugar, which previously had been 0.13 and 0.14, dropped within twenty-four hours to 0.073. Control children subjected to a similar withdrawal of carbohydrate from the diet failed to show any such change in the blood-sugar, the value remaining 0.13 and the children showing no signs of nausea or vomiting. These results are open to the criticism that the values found for the controls as well as for the subject of the experiment between attacks of vomiting are extremely high, being distinct examples of hyperglycemia. Since another author (Goetzky), working with the same method, obtained very much lower readings on many normal

11. Hilliger, G.: Ueber periodisches Erbrechen mit Acetonaemie, Jahrb. f. Kinderh., 1914, lxxx, No. 1.

children, the figures obtained by Hilliger in his vomiting case must be accepted with reserve. My own case shows an exactly opposite condition to that of Hilliger, for a percentage of 0.104 after so long a period of fasting would apparently point to a relative hyperglycemia, since, as pointed out by Mogwitz, the blood-sugar in starvation may fall to one-half its normal value. Further studies are being made in this case which will be reported on later.

The remaining cases are mostly those of children convalescing from different illnesses and show no variation from the normal.

In conclusion I wish to express my thanks to Professor S. R. Benedict for his kindness in placing this method at my disposal and for numerous helpful suggestions offered in the course of the work.

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A POCKET BABY SCALE*

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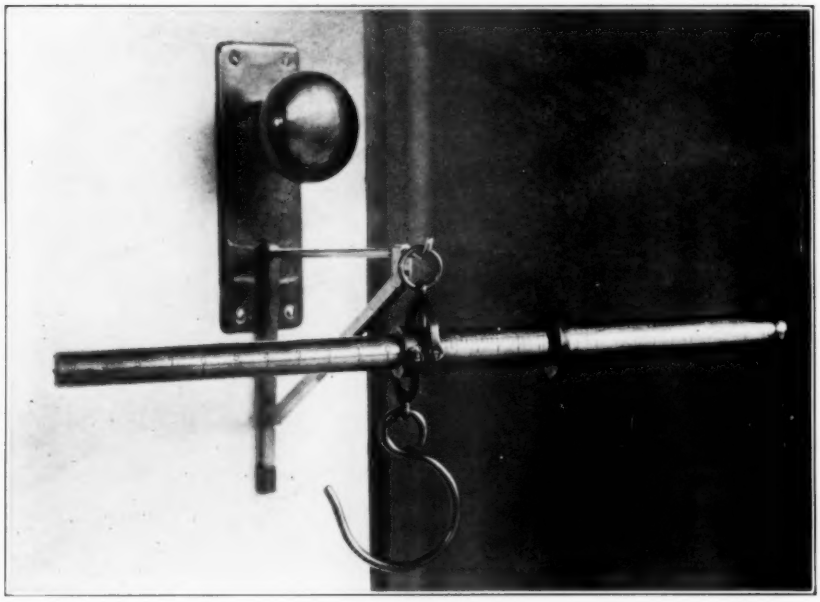
Every physician who has had to do with infant-feeding in private practice has realized the need of a means of ascertaining the weight of these little patients conveniently and accurately. In many families scales are to be found and records of the babies' weights are kept; but



A pocket baby scale.

usually no scale is available, or none is found that is sufficiently sensitive for all purposes. My experience with babies who are partially breast-fed and partially bottle-fed led me to search the market for a scale that would, by weighing the infant before and after nursing, show the amount it obtained from the breast. Any scale found that approached the necessary accuracy was so bulky and so poorly adapted to the purpose that I undertook to devise one to overcome these objections.

* Received for publication Nov. 20, 1914.

The one here described I have found satisfactory in every way. The principle of the old-fashioned steelyard is employed, the beam being so constructed as to telescope. The device, except the yokes and bearings, is made of brass, the telescoping core sliding through the tube in either direction. The divisions marked on the core represent pounds, while the scale on the tube is divided into ounces and quarters of an ounce, as indicated by the rider which traverses the entire length of tube. The yokes and bearings are of tempered tool steel and so constructed as to be sufficiently sensitive and yet insure unlimited service. A sight projecting from the tube and ranging with the arms of the upper yoke shows when the beam is level and in balance. A bracket whose members hinge and fold up closely is made to support the scale. The horizontal member of the bracket, when passed through the keyhole of a door, so engages as to hold it rigidly, thus leaving both hands free to attend to the weighing. The process then is as follows: The baby, slung in its napkin, is hung on the large hook; the core is slid to the mark indicating the number of pounds, and the rider completes the balance and indicates the ounces and fractions of an ounce. The capacity is 20 pounds. The scale and bracket are enclosed in a case measuring 1½ by 3 by 8 inches and altogether weigh 2 pounds.

Children's Memorial Hospital.

PROGRESS IN PEDIATRICS

REVIEW OF PROGRESS IN OPHTHALMOLOGY

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PREVENTION OF MYOPIA

Risley's well-known studies of refraction among the children of Philadelphia public schools in 1881 showed the presence of a high percentage of errors. Correction of these defects (and his results have been confirmed by others) proved the value of glasses not only in relieving symptoms and giving more acute vision but also in preventing increase of refraction. In other words, he has demonstrated that myopia is often acquired by the near use of uncorrected hyperopic astigmatic eyes.

The continued use of astigmatic eyes at the near point demands constant accommodation and convergence effort, and thus the eyes are laterally compressed by the internal and external recti muscles and are maintained in the state of refraction adapted to 13 inches, that is, a temporary myopia of 3 D. The combined effect of these two causes, especially in individuals who have inherited a tendency to stretching of the sclera, is to change the hyperopic astigmatism into myopic astigmatism at the opposite axis, and then by continuation of the use of the eyes under unchanged conditions the eyes become myopic in all meridians.

Risley's later publications (1913) of examination of nearly seven thousand eyes shows a steady decrease in the percentage of myopia. The moral to be drawn from this careful study of statistics and the truths clearly shown by them, is the necessity for the examination of all children's eyes under cycloplegia, and the accurate correction by glasses of errors of refraction. The modern class-rooms, the better distribution of light, the improved paper and print, and the stricter attention paid nowadays to the hygiene of the pupils and to the elimination from the schools of students with contagious conjunctivitis, contribute in no small degree to the betterment of both eyes and health.

During the present year the Committee of Conservation of Vision of the Pennsylvania State Medical Society has substantially aided the cause by having printed and permanently placed in schoolbooks used in Philadelphia public schools many thousand circulars, stating in easily understood language rules for the care of the eyes. The pre-

vention of myopia — and incidentally of some functional diseases and possibly of organic eye disease — is of incalculable value to any community.

PHLYCTENULAR KERATITIS AND CONJUNCTIVITIS

Phlyctenular keratitis and conjunctivitis in young persons are said to be ocular manifestations of tuberculosis. In order to determine the etiology of these two common affections the family history and the associated clinical appearances are of importance. The specific tests, such as von Pirquet's, while not alone sufficient to indicate general tuberculosis, are valuable sign-posts. In order that the skin reaction to tuberculin shall be reliable great care must be exercised, both as to the remedy itself and as to its method of application.

I exhibited at the Ophthalmic Section of the College of Physicians of Philadelphia four patients with suspected tubercular keratitis. In three the response to inoculation was prompt and strongly positive. In the fourth the reaction was negative, although general indications of diluted tuberculosis, such as swollen glands and malnutrition, were not wanting. The test was repeated in the negative case with greater accuracy and thoroughness and showed a strong reaction.

Boer[1] illustrates with cases the frequency with which a diagnosis of ocular tuberculosis may depend on the clinical appearance although the tubercle bacillus may not be demonstrated in the local lesion, and animal inoculation may prove negative. One case was that of a 21-months-old child, who during a severe conjunctivitis developed a thickening of the upper lid, which increased after recovery from the conjunctivitis. The condition was unilateral, ran a chronic course and was accompanied by marked thickening of the tarsus. The von Pirquet test was positive, and microscopic examination of excised tarsal tissue showed typical tubercles.

Butler[2] regards phlyctenular ophthalmia as the result of a "tuberculo-toxemia." A tuberculosis etiology was exceedingly probable in 70 per cent. of his cases. He has found that the symptoms disappear without other treatment within a couple of days after one injection of T. R.

Stephenson[3] in speaking of the diagnosis says that the advantages of the von Pirquet method are that it is safe and easily performed and is thus applicable for out-patients. On the other hand, the test is so sensitive, and tuberculosis past or present so common, that except in young children the positive reaction is not of much diagnostic use. The negative reaction is of greater value.

1. Boer: Arch. f. Ophth. (Graefe's) lxxxv, 1913, 273, 293, 362.
2. Butler: Brit. Med. Jour., Oct. 18, 1913.
3. Stephenson: Lancet, London, Nov. 29, 1913.

The Koch subcutaneous test gives both a general and a focal reaction. Stephenson draws one important distinction between the etiology of infection of the external portions, the conjunctiva, cornea and lacrimal apparatus, and infection of the iris and choroid and other parts of the interior of the eye. As a rule, he says, the former are exogenous, while the latter are endogenous. These facts are of value in prognosis, for while a tuberculosis lacrimal sac may be excised with good hope of extirpating the disease, excision of the eye with tubercle of the iris or choroid is likely to be of little value in eradicating or even in checking general tuberculosis.

On the other hand, phlyctenular ophthalmia is often a benign and transient complication or accompaniment of nasopharyngeal disease. Practitioners of extended experience and particularly those who commenced practice before the results of laboratory examinations were considered conclusive or even dependable, can remember cures effected by the removal of adenoids or enlarged tonsils to increase oxygenation of the blood, by restricted and nourishing diet and by the elimination of sources of intestinal irritation, and locally by astringent washes and emollient applications. Cobbledick[4] is convinced that adenoids are always present and claims that the result of promptly removing them, and, if necessary, the tonsils, is "magical." Further, any tendency to recurrence is said to disappear after the operation.

OPHTHALMIA NEONATORUM

The desirability of legislative enactment to prevent the ravages of ophthalmia neonatorum by early treatment has led to the formation of committees of medical men in many of the states of the United States. In Pennsylvania a law was passed about twelve or fifteen years ago requiring notice within six hours by midwives of redness of the lids or discharge from the conjunctiva in the new-born. In case of non-observance of this law a fine of two hundred dollars or imprisonment was to be exacted. Apparently the law in Pennsylvania — and this is equally true of other states — becomes a dead letter unless breakers of the law are convicted. In the few weeks following a conviction the number of cases reported increases amazingly and then it gradually drops off until a new violation is discovered and the culprit punished. New measures will probably be no more effective unless all avenues for the escape of violators be closed, and this fact should not be forgotten by the framers of the laws.

The following paragraph[5] from the *Journal of the American Medical Association* is apropos here:

4. Cobbledick: Brit. Med. Jour., Nov. 22, 1913.
5. Jour. Am. Med. Assn., Oct. 17, 1914, p. 1392.

The prevention of this disease, so serious for the babe's future, is not attained by discussing the value of eugenics, or attempting the regulation of prostitutes, or demanding the always non-successful reporting of gonorrheal cases. It will be more certainly secured by insisting that every physician and every midwife (by continued and repeated instruction) shall use Credé's method, namely, to instil into each eye of every new-born babe two drops of a 2 per cent. solution of silver nitrate. Every eye inflammation in the new-born, or occurring shortly after birth, should be considered ophthalmia until the microscope shows that it is an innocent inflammation. If the gonococci are found, the little patient should be placed in the care of a skilled oculist.

It must be borne in mind that gonococci are not essential to the production of purulent ophthalmia and that their absence does not always prove that the eye is free from danger. On the contrary, many cases of severe ophthalmia bearing all the clinical signs of gonorrheal inflammation but without laboratory confirmation lead to ulceration and destruction of the cornea. At times one may be led to suspect carelessness or ignorance of the microscopist, so inconsistent are his findings with the violence of the symptoms.

Holloway[6] writes:

It is now quite generally known that many of these cases are non-gonorrheal in origin, and for reasons that are obvious, the proportion of gonorrheal cases, both in and out of institutions, necessarily varies according to the social and moral character of the patients.

From the studies of Stephenson, Mayou and others, it is safe to assume that 60 per cent. to 65 per cent. of the cases owe their origin to a Neisser infection, although some recent writers, for example Sattler (Am. Oph. Soc., 1913) concede but 50 per cent. We thus see that many of these cases may be regarded as cases of purulent ophthalmia analogous to those seen in association with some of the infectious diseases of children.

PROPHYLAXIS

Sattler says:

We have a fairly reliable prophylaxis for non-specific organisms, but a next to impossible one for specific or gonococci. The latter infection will continue undisturbed its destructive work and defy the best prophylactic measures at present at our command and claim their quota of infantile eyes.

Notwithstanding this pessimistic statement, and in view of the unquestioned truth that the number of cases of ophthalmia of the new-born has been enormously reduced since the almost universal adoption of the Credé method, it becomes the duty of every obstetrician to sterilize both the birth canal and the infant's eyes.

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6. Holloway: Ophth. Rec., December, 1913.

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